MEDICAL TIMES

Vol. 78 July 1950 No. 7

a **new**
antibacterial
agent . . .

Wide antibacterial activity, low toxicity and virtual elimination of renal complications distinguish the use of Gantrisin* 'Roche', a new and remarkably soluble sulfonamide. Highly effective in urinary as well as systemic infections, Gantrisin does not require alkali therapy because it is soluble even in mildly acid urine. More than 20 articles in the recent literature attest its high therapeutic value and the low incidence of side-effects. Gantrisin is now available in 0.5 Gm tablets, as a syrup, and in ampuls. Additional information on request.

HOFFMANN-LA ROCHE INC • NUTLEY 10 • N. J.

Gantrisin®

* *Brand of sulfisoxazole (3,4-dimethyl-5-sulfanilamido-isoxazole)*

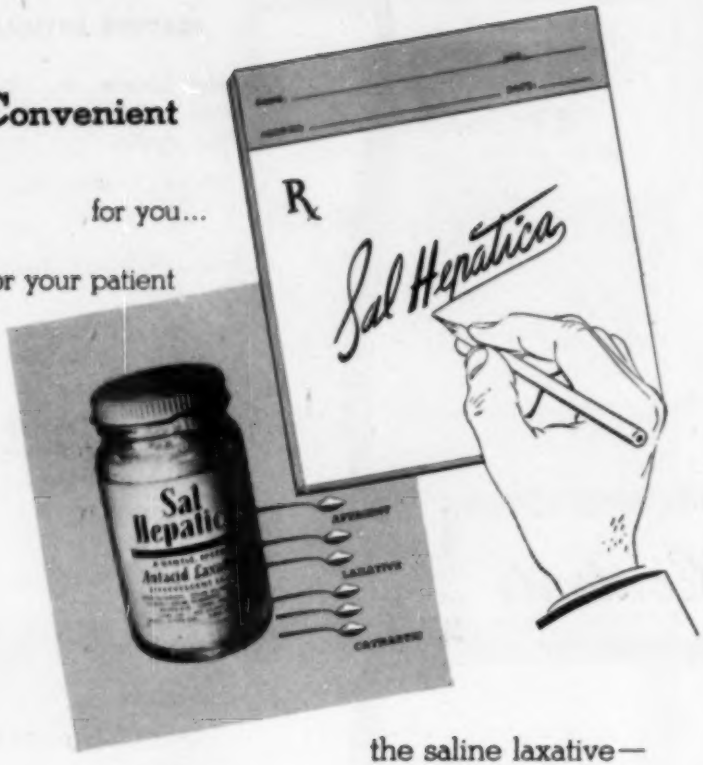
'Roche'

Contents

Convenient

for you...

for your patient



the saline laxative—

Whether your patient needs a laxative, or an aperient, or a cathartic you'll find it more convenient to write SAL HEPATICA on your prescription pad. No need to specify all the ingredients of three separate formulas, just prescribe SAL HEPATICA and indicate the dosage.

Your patients will find SAL HEPATICA convenient, too. No cluttering of shelves with bottles of different laxatives when one will serve. They'll like its pleasant taste, its effervescence—and, of course, its prompt, gentle action.

a product of **BRISTOL-MYERS** • **19 West 50 Street, New York 20, N. Y.**

Contents

the oral route is the simplest

For maintaining the edema-free state, here—at last—is truly effective oral mercurial diuretic therapy. One or two Tablets MERCUHYDRIN® with Ascorbic Acid daily (more when indicated) generally controls cardiac edema with

greater convenience · greater economy · greater safety

tablets MERCUHYDRIN

WITH ASCORBIC ACID

After parenteral therapy, your patient has been brought to unfluctuating basic weight. Then systematic oral therapy employing Tablets MERCUHYDRIN (brand of meralluride) with Ascorbic Acid may eliminate the need for injections entirely in mild decompensation. In more advanced cases, you can greatly reduce the number of injections required to maintain your patients free of edema.

Prolongation of the interval between injections simplifies management. The diuretic response is good, the tablets are well tolerated, the method is convenient, and the economy considerable.

Packaging: Tablets MERCUHYDRIN with Ascorbic Acid, available in bottles of 100 tablets. Each tablet contains meralluride 60 mg. (equivalent to 19.5 mg. mercury) and ascorbic acid 100 mg.

Lakeside Laboratories, INC.

MILWAUKEE 1, WISCONSIN

Medical Book News

save **68** *more fetal lives in habitual abortion, threatened abortion and premature labor*

des

A review of the pertinent literature reveals that while the administration of diethylstilbestrol (**des**) will bring 86.6% of cases to term (1), progesterone will bring only 18.2% to term (2), a very significant difference of 68.4%. Karnaky (3) found in his study of 35 women who were treated with massive doses of **des** that all pregnancies carried to term. This evidence shows that at least 68.4% more fetal lives may be saved with **des.**

des is specifically designed for the treatment of threatened abortion, habitual abortion and premature labor. **des** tablets dissolve within a few seconds and are uniformly absorbed into the blood stream. Adequate dosage of **des** administered early in premature labor stops the pain in less than one minute.

des 25 mg. tablets of Grant Process highly micronized triple crystallized diethylstilbestrol U.S.P. XIII are available in containers of 30, 100, and 500 tablets.

save **68** *more fetal lives*

NOW! FOR PARENTERAL ADMINISTRATION

Bio-des

FOR INTRAMUSCULAR INJECTION

Bio-des (des in oil) contains 25 mg. per cc. of Grant Process micronized diethylstilbestrol U.S.P. XIII in redistilled sesame oil.

Bio-des is available in vials of 10cc. and 30cc.

REFERENCES:

(1) Rosenblum, G. and Melinkoff, E. Preservation of the Threatened Pregnancy with Particular Reference to the Use of Diethylstilbestrol. West. Jr. Surg. Obs. and Gyn. 55, 597-603. Nov. 1947.

(2) Silbernagel, W. M. and Burt, O. P. Ohio State Med. Jr. 39, 430, May 1943.

(3) Karnaky, K. J. Estrogenic Tolerance in Pregnant Women. Amer. Jr. Obs. and Gyn. 53, 312-316, 1947.

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Grant Chemical Company, Inc.

95 MADISON AVENUE, NEW YORK 16, NEW YORK

MEDICAL TIMES

THE JOURNAL OF GENERAL PRACTICE

Incorporating the

LONG ISLAND MEDICAL JOURNAL

WESTERN MEDICAL TIMES

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Therapy for the common anemias — THE SQUIBB VITAMIN B_{12} FAMILY

	VITAMIN B_{12} (*micrograms*)	FOLIC ACID (*milligrams*)	FERROUS SULFATE *Exsiccated* (*milligrams*)	ASCORBIC ACID (*milligrams*)	DOSAGE		SUPPLY
					THERAPEUTIC	MAINTENANCE	
oral **RUBRAFERATE** *per Capsule*	4.17	0.28	130	50	2 Capsules t.i.d.	1 Capsule t.i.d.	Bottles of 100
oral **RUBRAFOLIN** *per Capsule*	25	1.67			1 Capsule daily	1 Capsule daily	Bottles of 100
oral **RUBRAMIN** *per Capsule*	25				6 to 12 Capsules daily	(see note)	Bottles of 100
parenteral **RUBRAMIN**— *Squibb Vitamin B_{12} Concentrate per cc.*	15 & 30				15 to 30 micrograms once or twice a week	15 to 30 micrograms once or twice a month	1 cc. ampuls, 15 and 30 micrograms per ampul. 5 and 10 cc. vials, 30 micrograms per cc.

NOTE: The above are average dosages. As with any antianemia preparation, dosages must be adjusted to the needs of the individual patient.

Maintenance dosages of oral vitamin B_{12} alone must be adjusted to the patient's needs. Response to oral vitamin B_{12} alone varies greatly from patient to patient and from time to time in the same patient.

Also available—Solution Rubramin Crystalline (Squibb Crystalline Vitamin B_{12} Solution) in 1 cc. ampuls, 15 micrograms of Crystalline Vitamin B_{12} per ampul. 10 cc. vials, 30 micrograms per cc.

SQUIBB

Board of Contributing Editors

appetite must be controlled

"The greatest problem in preventive medicine in the United States today is obesity."[1] And today it is well-known that "*The only way to counteract obesity . . . is by a restriction of food intake.*"[2]

'Dexedrine' Sulfate controls appetite, making it easy for the patient to avoid overeating and thus to lose weight safely without the use (and risk) of such potentially dangerous drugs as thyroid. In weight reduction 'Dexedrine' "*is the drug of choice because of its effectiveness and the low incidence of undesirable side effects.*"[1]
Smith, Kline & French Laboratories • Philadelphia

Dexedrine* Sulfate tablets • elixir

A most effective drug for control of appetite in weight reduction

*T.M. Reg. U.S. Pat. Off. for dextro-amphetamine sulfate, S.K.F.

1. Walker, W.J.: Obesity as a Problem in Preventive Medicine, U.S. Armed Forces M.J. 1:393, 1950.

2. John, H.J.: Dietary Invalidism, Ann. Int. Med. 32:595, 1950.

CHLOR-TRIMETON

Ace in the hole...

Chlor-*Trimeton** is so potent, so much more effective in alleviating allergic symptoms, especially those due to hay fever, vasomotor rhinitis and urticaria, that more and more physicians turn to it when other antihistaminic compounds give only partial relief or fail entirely. No patient should be classed as unresponsive to antihistamines until Chlor-*Trimeton* has been tried.

CHLOR-*TRIMETON*
MALEATE

(brand of chlorprophenpyridamine maleate)

Chlor-*Trimeton*, most potent antihistaminic agent available, acts rapidly, providing relief in 20 to 30 minutes. Depending upon the nature of the allergic disorder and its intensity, symptomatic control is maintained from four to six hours. Side effects occur in less than 10 per cent of patients. Because Chlor-*Trimeton* is remarkably efficient, it would seem desirable to prescribe it first in all new patients requiring antihistamines.

Packaging: Chlor-*Trimeton* Maleate (chlorprophenpyridamine maleate) 4 mg. tablets. Bottles of 100 and 1000 scored tablets tinted yellow for identification. Chlor-*Trimeton* Maleate Syrup (brand of chlorprophenpyridamine maleate) containing 2 mg. per 4 cc. (1 teaspoonful) is available in bottles of 16 oz.

*T.M.

Schering CORPORATION • BLOOMFIELD, NEW JERSEY

SCHERING INC

When Hyperacidity is a problem—

ANTACID

SEDATION

SPASMOLYSIS

Silaloid Tablets

ANTACID THERAPY can be as impracticable as a one legged stool. Too often the influence of the psychogenic component is overlooked in concern with gastric and intestinal pain.

Silaloid provides a *palatable* and *practical*, over-all therapeutic answer to conditions ranging from hyperacidity to gastric and peptic ulcers. Silaloid can be swallowed, chewed or taken in a glass of water, where it disintegrates rapidly—in a few seconds.

Each SILALOID tablet contains:

ANTACID	*7 gr. magnesium trisilicate*—a non-systemic, non-constipating antacid sufficient to neutralize 45 cc. of 0.1 N. HCl.
SEDATIVE	*½ gr. phenobarbital*—to decrease tonus of the intestinal musculature and to provide central depressant action on the vagus.
ANTISPASMODIC	*1/1250 gr. hyoscyamine sulfate, 1/5000 gr. atropine sulfate*—to control excessive motor activity, hyperperistalsis and pylorospasm.

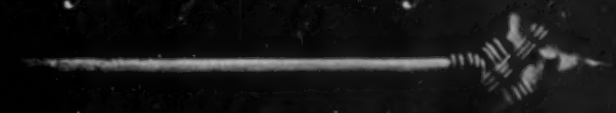
In your patients requiring antacid therapy, prescribe Silaloid for its prompt and prolonged action and its over-all rationale.

DOSAGE: *Two tablets 3 to 4 times daily or as required.*

SUPPLIED: *In bottles of 100, 500, 1000 tablets.*

VANPELT & BROWN, INC., *Pharmaceutical Chemists* **Richmond, Virginia**

Quickly and surely



attack the Attack

For the asthmatic or cardiac patient, AMINET Suppositories present definite advantages over ordinary aminophylline suppositories:

The unique Bischoff base (without cocoa butter) prevents inactivation of the active ingredients and favors more rapid absorption. Potency is protected and stability is assured.

AMINET® *Suppositories*

are always therapeutically fresh and melt at body temperature

The combination of aminophylline and pentobarbital sodium, readily absorbed by rectum, quickly relaxes the bronchi, calms the patient and allays anxiety and apprehension. Relief—in a matter of minutes—is prompt with AMINET Suppositories, and is prolonged for hours. Response is excellent, even in epinephrine-fast patients.

Since AMINET Suppositories are easily administered by the patient himself at the first indication of an impending attack, they are highly useful in acute bronchial asthma, as well as seasonal asthma, cardiac asthma (paroxysmal nocturnal dyspnea) and Cheyne-Stokes respiration. Tolerance to AMINET Suppositories is greater than to aminophylline injections.

AMINET Suppositories are available in:

Full Strength containing Aminophylline 0.5 Gm. (gr. 7½) and Pentobarbital Sodium 0.1 Gm. (gr. 1½)

Half Strength containing Aminophylline 0.25 Gm. (gr. 3¾) and Pentobarbital Sodium 0.05 Gm. (gr. ¾)

Benzocaine has been added for its anesthetic effect.

Bischoff

ERNST BISCHOFF COMPANY, INC. • BRIDGEPORT, CONN.

Patient under Treatment

FOR CHRONIC URINARY TRACT INFECTION

ENJOYS

Gratifying Relief

from distressing symptoms

Urinary frequency and pain and burning on urination can be relieved promptly in a high percentage of patients throughout the course of specific treatment, by the oral administration of Pyridium.

This effective urinary analgesic is safe, virtually nontoxic, and has no systemic sedative or narcotic action. Pyridium has proved to be a valuable adjunct to specific therapy in prostatitis, cystitis, urethritis, and pyelonephritis.

Pyridium is the trade-mark of Nepera Chemical Co., Inc., successor to Pyridium Corporation, for its brand of phenylazo-diamino-pyridine HCl. Merck & Co., Inc. sole distributor in the United States.

The complete story of Pyridium and its clinical uses is available upon request.

Pyridium®

(Brand of phenylazo-diamino-pyridine HCl)

MERCK & CO., INC. *Manufacturing Chemists* RAHWAY, NEW JERSEY

In Canada: MERCK & CO. Limited—Montreal, Que.

NO WONDER SO MANY DOCTORS THROUGHOUT THE NATION PRESCRIBE

The Stuart Hematinic

COMPARE

THESE HIGH POTENCIES* OF IRON, COPPER, B COMPLEX AND C

THE STUART HEMATINIC	CONTENTS PER TABLET	CONTENTS PER 6 TABLETS
FERROUS GLUCONATE	3 grs.	18 grs.
COPPER SULPHATE	2.5 mg.	15 mg.
B COMPLEX		
Liver Fraction (alcohol insoluble—natural B Complex)	6 grs.	36 grs.
Thiamin Chloride	3.3 mg.	20 mg.
Riboflavin	1.7 mg.	10 mg.
Niacin Amide	25 mg.	150 mg.
Calcium Pantothenate	1.7 mg.	10 mg.
Pyridoxin Hydrochloride	0.5 mg.	3 mg.
VITAMIN C	25 mg.	150 mg.

DOSE: one or two tablets after each meal

PLUS:

LOW COST TO YOUR PATIENTS

BOTTLE OF 100 CAPSULE-SHAPED TABLETS **$2.95**

PLUS:

THESE OTHER ADVANTAGES

Contains Ferrous Gluconate (better tolerated—greater iron utilization**). Contains Liver Fraction for Natural B Complex. Unique tablet structure separates all the non-compatible substances for complete stability. Tablets disintegrate gradually in the stomach, releasing iron at a desirable rate.

Also Available

The STUART HEMATINIC with FOLIC ACID

...the same as the Stuart Hematinic except for the addition of 4.5 mg. of Folic Acid per 6 tablets.

Bottle of 100 capsule-shaped tablets, $3.85

*Potencies and balance cover latest standards for multiple therapeutic dosage. 1. *Rehabilitation Through Better Nutrition*, 1947—Spies. 2. *Journal of American Medical Association*, Oct. 27, 1945; 129:613—Jolliffe. 3. *Vitamin Deficiencies: Stigmen, Symptoms and Therapy* (J. A. M. A., June 23, 1945, 131:666—Council on Foods and Nutrition). 4. *Clinical Hematology*, Dec. 1946, Pg. 349—M. M. Wintrobe. ** *Journal of Clinical Investigation*, 16:547-54, 1937—Paul Reznikoff and W. F. Goebel.

New Relief in Hay Fever

Antistine-Privine
NASAL SOLUTION

A synergistic combination of an Antihistaminic and Vasoconstrictor

ANTISTINE-PRIVINE gives prompt, prolonged relief from allergic nasal congestion.

This new synergistic combination contains the effective antihistaminic, ANTISTINE, to block the congestive action of histamine, and the potent vasoconstrictor, PRIVINE, to shrink the nasal mucosa.

It has been established that "the decongestive action of ANTISTINE-PRIVINE on the allergic nasal mucosa in many instances appears to be more intense and prolonged than from either solution alone."[1]

PRIVINE is still available for use in those conditions where the antihistaminic component is considered unnecessary.

ANTISTINE-PRIVINE, aqueous solution of Antistine hydrochloride 0.5%, and Privine hydrochloride, 0.025%, in bottles of 1 fl. oz. with dropper.

DOSAGE: 2 to 3 drops in each nostril 3 or 4 times daily. PRIVINE hydrochloride, 0.05% solution in 1 pint and 1 oz. dropper bottles for prescription; 0.1% solution reserved for office procedures, in 1 pint bottles only.

1. Friedlaender & Friedlaender: Amer. Pract. 2:543, June, 1948

Ciba PHARMACEUTICAL PRODUCTS, INC., SUMMIT, NEW JERSEY

ANTISTINE® (brand of antazoline); PRIVINE® (brand of naphazoline) 2/1861M

For Rapid Disinfection of Instruments

CHLOROPHENYL

Affords a Valuable Instrument Disinfecting Medium for WARD and PROFESSIONAL OFFICE Use

This powerful disinfecting solution is free from phenol (carbolic acid) and mercurials. It is a chlorinated phenyl compound that is unusually effective in its rapid destruction of commonly encountered vegetative bacteria (except tubercle bacilli) as shown in the chart.

PRICE
Per Gallon . $5.00
Per Quart . $1.75

B-P instrument container No. 300 is recommended as the ideal office container for use with the Solution.

Check these additional features—

- Non-injurious to metallic instruments or keen surgical edges.
- Low volatility ... will not irritate eyes, nose or throat.
- Will not stain fabrics, skin or tissue.
- Will not dry and fissure hands or skin areas if exposed repeatedly. (Chlorophenyl is not to be used therapeutically.)
- Stable ... will retain potency over long periods.

Compare the killing time of this superior bactericidal agent

Vegetative Bacteria	50% Dried Blood	Without Blood
Staph. aureus	15 min.	2 min.
E. coli	15 min.	3 min.
Strept. hemolyticus	15 min.	15 sec.

Ask your dealer

PARKER, WHITE & HEYL, INC.
Danbury, Connecticut

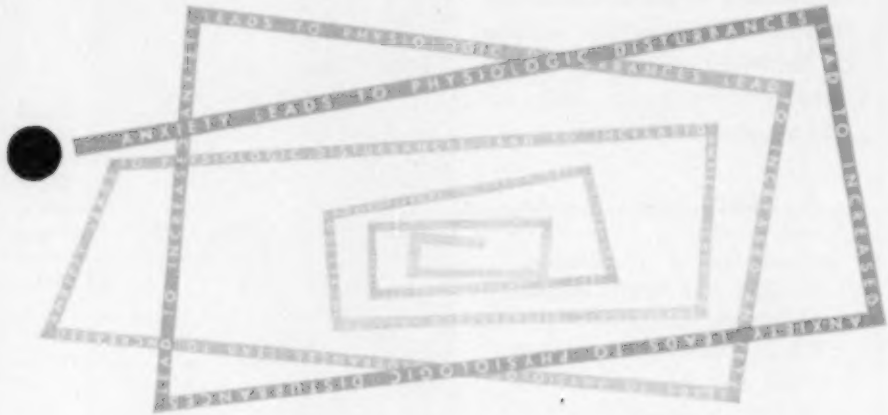
B-P

A BARD-PARKER PRODUCT

SEDAMYL

[ACETYLBROMDIETHYLACETYLCARBAMID SCHENLEY]

helps the patient escape from the psychosomatic maze



in anxiety states

sedation without hypnosis

ideal for daytime use...

SEDAMYL is not a barbiturate. Professional literature and samples on request.

Because SEDAMYL® quickly helps overcome anxiety, apprehension, and nervousness without causing drowsiness, "hangover", or impaired perception, it is considered ideal for low-level daytime sedation. Under the gentle influence of SEDAMYL, the patient feels as though he is having one of his "good" days.

SEDAMYL is quickly absorbed, affording rapid and full response. Readily metabolized, it is well tolerated in therapeutic doses and does not produce undesirable circulatory or respiratory effects.

SUPPLIED: Tubes containing 20 tablets; bottles containing 100 tablets; each tablet provides 0.20 Gm. (4 gr.) of acetylbromdiethylacetylcarbamid.

SCHENLEY LABORATORIES, INC., 350 Fifth Ave., New York 1

LETTERS

TO THE EDITOR

This department is offered as an Open Forum for the discussion of topical medical issues. All letters must be signed. However, to protect the identity of writers, who are invited to comment on controversial subjects, names will be omitted when requested.

HEALTH BILL

"A recent article in the CLEVELAND PLAIN DEALER concerning the 'health bill' contained a typographical error of the type that comes easy these days. Three zeros, by themselves, don't add up to much, but in the spot where they were missing in your article they make the difference between $17,000,000,000 and $17,000,000.

"Not that any of us has much conception of how much a billion amounts to, but it does represent the main objection to the health bill as proposed. The Brooking's Institution estimate of $17,000,000,000 a year for the compulsory health tax program is higher than the administration's estimate and lower than several other informed guesses, but all credible estimates underline the fact that it would call for a completely unwarranted outlay of funds for anything short of a perfect plan, and the present plan is so full of inadequacies, holes, creaking joints and political pork that it is a burden no taxpayer should want to assume."

Russell B. Roth, M.D.
Erie, Pa.

A PHARM. MFR. REPORTS ON BRITAIN'S SOCIALIZED MEDICINE

"In a recent talk before the Pharmaceutical Advertising Club of New York I tried to emphasize that too many of us are adopting the attitude that socialized medicine is inevitable and consequently are doing nothing about it.

—Continued on page 30a

forestall capillary hemorrhage

Hesperidin-C, a combination of hesperidin and ascorbic acid, improves capillary strength in from 85 to 90 per cent of cases with abnormal fragility.[1,2,3] This clinical response is not exhibited by any vitamin P substance alone.

Hesperidin-C

for abnormal capillary fragility and permeability

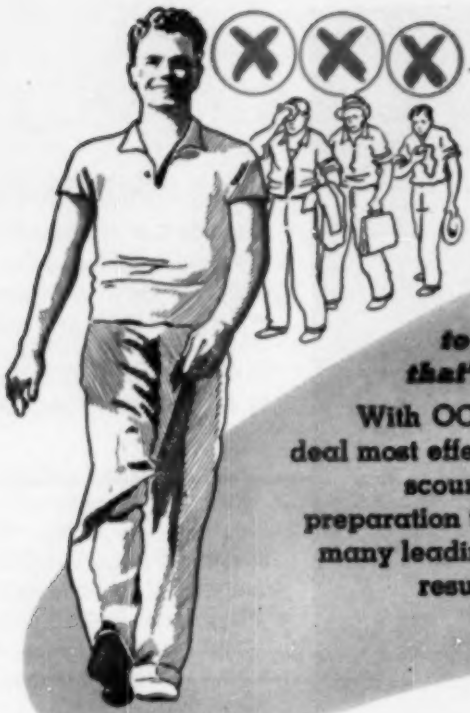
Hesperidin-C is indicated in many clinical conditions encountered in daily practice—hypertension, purpura, diabetes, scurvy, radiation damage. As a therapeutic or prophylactic adjunct, *Hesperidin-C* will lessen the danger of such complications as apoplexy, coronary occlusion, retinal hemorrhage and sensitivity reactions resulting from abnormal capillary permeability or fragility.

Dosage: 1 to 3 tablets or capsules twice daily. Each tablet or capsule represents hesperidin 50 mg. and ascorbic acid 50 mg.

1. Barishaw, S. B.: Exper. Med. & Surg. 3:358, 1949.
2. Loughlin, W. C.: N. Y. State M. J. 49:1823, 1949.
3. Selsman, G. J. V.: To be published.

More than Half a Century of Service to the Medical Profession

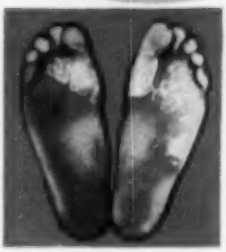
The National Drug Company
Philadelphia 44 Pa.



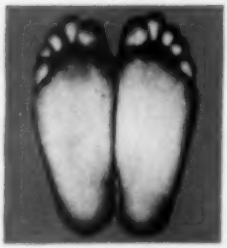
SUMMER

3 out of 4 are bound to catch athlete's foot*— that's summer's usual toll!

With OCTOFEN, you're ready to deal most effectively with this summer scourge—for OCTOFEN is the preparation that's won the acclaim of many leading specialists for brilliant results in many clinical tests.



BEFORE
Athlete's foot 12 years' duration.



AFTER
Clear after 3 months' of treatment.

1½ & 4 Ounce Bottles For Your Rx Convenience

*Mod. Med. Topics, 10:7, July, 1949.

The Superiority of Octofen is measured in feet

51 Difficult Dermatologic Cases Treated With Tarbonis Showed These Remarkable Results[1]

	CASES	CLEARED or MARKED IMPROVEMENT	MODERATE IMPROVEMENT	SLIGHT or NO IMPROVEMENT
PSORIASIS	11	2	4	5
NEURODERMATITIS	5	3	2	-
ATOPIC ECZEMA	8	6	1	1
SEBORRHEIC DERMATITIS	6	5	1	-
CHRONIC RECURRENT CONTACT DERMATITIS	11	9	1	1
VARICOSE ECZEMA	4	1	1	2
ALLERGIC DERMATITIS	3	-	2	1
LICHEN PLANUS	3	2	1	-
TOTAL	51	28	13	10
%		54.9	25.5	19.6

In 41 of these cases, the condition had persisted for 2 to 10 years, not yielding to other forms of therapy.

Treatment with TARBONIS over a 5-week to 5-month period showed that 54.9% of the cases cleared or showed marked improvement, while 25.5% showed good response. TARBONIS, the original clean, white coal tar cream, gave satisfactory results in 80.4% of these patients!

1. Lowenfish, F. P., N. Y. State J. Med., 50:922 (Apr. 1) 1950.

All the therapeutic advantages of crude coal tar with irritating residues removed; higher in active fractions of coal tar; homogenized for perfect emulsification.

For prescriptions — all pharmacies stock 2¼-oz. and 8-oz. jars; for dispensing purposes, 1-lb. and 6-lb. jars are available through your surgical supply dealer.

THE TARBONIS COMPANY Dept. M.T.
4300 Euclid Ave., Cleveland 3, Ohio

Please send me literature and clinical sample of TARBONIS.

_____ M.D.

Address _____

City _____ Zone ____ State ____

a major step
in rehabilitation of the
parkinsonian patient

PANPARNIT T.M.

Known previously to investigators as PARPANIT.

Treatment of the Parkinsonian syndrome with PANPARNIT was observed by Schwab and Leigh[1] "to be superior to the previous medication" in 65% of cases. With a careful regimen of gradually increasing dosage, "very satisfactory results with this new compound will follow."

By reducing rigidity and tremor PANPARNIT frequently enables the Parkinsonian patient to resume a more nearly normal life . . . to perform simple daily tasks, to feed, to shave, and to dress himself. Improvement of physical status leads to increasing self-reliance and a happier frame of mind—a major step toward mental as well as physical rehabilitation.

A totally new synthetic drug, PANPARNIT offers the advantages over the belladonna alkaloids of frequently affording more satisfactory relief and rarely causing disturbances of vision or dryness of the mouth.

1. Schwab, R. S. and Leigh, D.: J.A.M.A. *139*:629, 1949.

Geigy

Fuller information regarding clinical studies and suggested dose schedules will be furnished gladly.

PANPARNIT (caramiphen hydrochloride): Available as sugar-coated tablets 12.5 mg. (bottles of 100) and 50 mg. (bottles of 50, 250 and 1000).

GEIGY COMPANY, INC., 89-91 Barclay St., New York, N. Y.

NEW...

A Positive Approach in the Medical Management of PEPTIC ULCER

ALLUCEE

PATENT PENDING

ALLANTOIN, ASCORBIC ACID, AND ALUMINUM HYDROXIDE GEL—KREMERS-URBAN

More than just another antacid or protectant, ALLUCEE* actually promotes faster, better healing of the ulcer, while it aids in controlling the distress of hyperacidity. One ALLUCEE capsule provides:

ALLANTOIN 60 mg.	*To stimulate granulation and accelerate healing*
ASCORBIC ACID 50 mg.	*To strengthen scar tissue and reduce capillary fragility*
ALUMINUM HYDROXIDE GEL (Dried) U. S. P. 100 mg.	*To enhance the buffering and protectant action of gastric mucin*

SUPPLIED: Bottles containing 100 and 1,000 capsules. Literature and samples on request.

*Trademark of Kremers-Urban Co.

K-U

Kremers-Urban Co.

Pharmaceutical Chemists Since 1904

MILWAUKEE 1, WISCONSIN

LETTERS

continued
from page 22a

"The 1949 Ochsner Clinic Report of 500 consecutive admissions reveals that 386 patients or 77 per cent were psychosomatically ill. Their mental attitude created a condition of illness. A fatalistic policy of inaction can very well bring on government control of medicine—nationalization of the chemical and pharmaceutical industry would of course follow.

"Two months before the English National Health Service program began 87 per cent of all physicians in Great Britain were against the plan. Within a month after N.H.S. was instituted, 87 per cent were still against it, although 90 per cent had signed up because they felt they had to. The English medical profession made no real fight to defend themselves and just let N.H.S. happen. Evidently they felt it was inevitable.

"It is this reflected aura of inevitability in our thinking which prompts me to state emphatically that I am opposed to government control of any kind whatsoever over the health problems of the U.S.A., and this in spite of a tremendous increase in the sale of our tonic in England under N.H.S. This is normally supplied in 7-oz. and 14-oz. sizes. The N.H.S. physician began prescribing 'Winchesters' (two quarts). From Winchesters they went to gallons—their attitude being if the patient needs a tonic today he will need it tomorrow. I understood this attitude after visiting a classmate of mine now practicing in Preston, Lancaster, and found he was seeing 15-22 patients an hour during office hours in addition to 29-33 house calls a day.

"Sir Stafford Cripps, Chancellor of the Exchequer, evidently does not believe in N.H.S. for on July 19th, 1949, he entered a clinic in Switzerland to undergo six weeks' treatment for a digestive complaint. I wondered why he elected to pay for his

—Continued on page 34a

SURFACE TENSION

The carefully adjusted, low surface tension of Koromex Jelly and Cream, assures even spreading over the entire vaginal mucosa. This results in greater penetration, increased barrier action and faster spermicidal time.

ACTIVE INGREDIENTS: BORIC ACID 2.0% OXYQUINOLIN BENZOATE 0.02% AND PHENYLMERCURIC ACETATE 0.02% IN SUITABLE JELLY OR CREAM BASES

KOROMEX

A CHOICE OF PHYSICIANS

HOLLAND-RANTOS COMPANY, INC. • 143 HUDSON STREET, NEW YORK 13, N. Y.

MERLE L. YOUNGS
PRESIDENT

RELAX THAT SPASM with MESOPIN

When pain, heartburn, belching, nausea, or unstable colon are due to gastrointestinal spasm, Mesopin provides an effective means for prompt relief. Its selective antispasmodic action on the digestive tract controls spasticity without the undesirable side effects of atropine or belladonna. Thus, symptomatic relief of many common disturbances of the stomach or intestines can be achieved with discrimination and safety. Mesopin is indicated for the relief of gastrointestinal spasticity, such as pylorospasm, cardiospasm, spastic colon, and biliary spasm.

MESOPIN (brand of homatropine methyl bromide)

SELECTIVE GASTROINTESTINAL ANTISPASMODIC

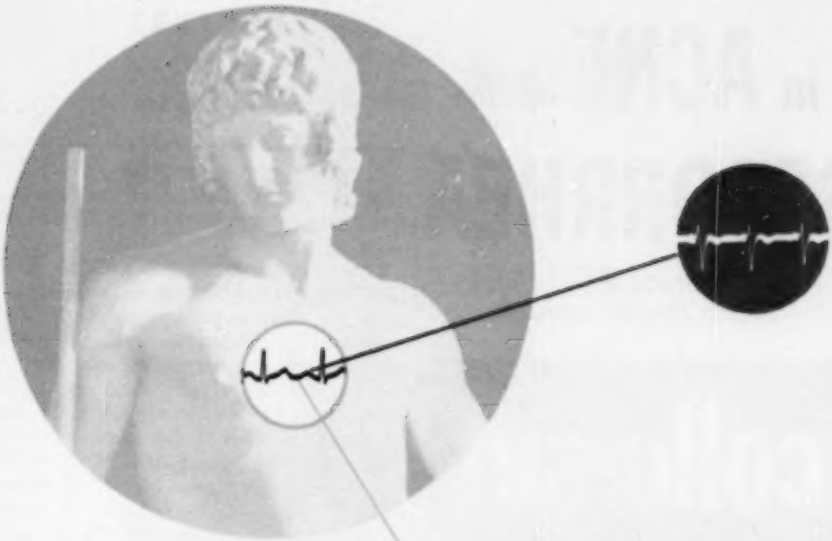
SUPPLY: Elixir in 16 ounce bottles; tablets in bottles of 100.
MESOPIN (homatropine methyl bromide)—2.5 mg. per teaspoonful of elixir or per tablet. Also supplied: MESOPIN-PB*—2.5 mg. Mesopin and 15 mg. (1/4 gr.) phenobarbital per teaspoonful of elixir or per tablet.

Detailed literature and samples on request.

Endo®

*PB abbreviated designation for phenobarbital.

ENDO PRODUCTS INC., RICHMOND HILL 18, NEW YORK



IN SEVERE HYPERTENSION

complicated by cardiac failure

The effects of VERTAVIS (veratrum viride, Irwin-Neisler) in severely hypertensive patients, including some with cardiac failure, now "warrants the hope that such patients may receive lasting benefit from this therapy."[1] In resistant cases, VERTAVIS was responsible for more normal and efficient myocardial action, relief of exertional dyspnea and palpitation . . . and the most marked reduction in blood pressure of all drugs previously used in essential hypertension.[1,2] "Prolonged therapy in some cases resulted in a diminution in cardiac size and reversal of electrocardiographic changes toward normal."[1]

VERTAVIS contains in each tablet: veratrum viride Biologically Standardized, 10 CRAW UNITS. The CRAW UNIT of potency is an Irwin-Neisler research development. For more complete information, see pages 439-440 of your 1950 Physicians' Desk Reference (PDR).

Vertavis®
(IRWIN-NEISLER)

(1) Freis, E. D., and Stanton, J. R.: Am. Heart J. 36: 723-738, 1948; (2) Freis, E. D.: Med. Clin. N. Am. 32: 1247-1258, 1948.

IRWIN, NEISLER & COMPANY **DECATUR, ILLINOIS**

LETTERS

continued from page 30a

treatment in Switzerland rather than accept treatment under the N.H.S. plan in Great Britain.

"I was inclined to agree with Sir Stafford Cripps after visiting an associate of mine, Dr. Francis Johnson, while he was a patient in a London hospital. Dr. Johnson, hemorrhaging internally, was taken to the hospital by his wife late one night (3:30 A.M.). An ambulance could not be dispatched without the necessary forms from his N.H.S. physician! Two weeks after he had entered the hospital, I visited him. During our conversation I asked about X-rays. He smiled slightly and said that except for the first few hours after he first was admitted, no physician had attended him. They were too busy. An intern was attempting to prescribe a diet, but as yet no medication had been prescribed. While I was at the bedside a tea wagon was rolled up by an attendant, who very gaily said: 'There you are Guv'ner, sip your tea while it's hot, and these cigarettes are compliments of the government. God bless the N.H.S., eh wot!' Four years previous to this, Dr. Johnson had been operated on for stomach ulcers. Dr. Johnson, with a rather knowing look, stated: "The intern told him to be sure and give me my tea morning and afternoon, and I do enjoy the cigarettes so much.'

"While in England I spoke to many people, including hotel porters, taxicab drivers, lorry drivers, bookkeepers, accountants, shipping clerks, advertising executives, bankers, and business men at various levels. In every discussion I had concerning N.H.S., I tried to let the Englishman talk so that I could obtain his views, rather than ask any leading questions. Invariably the following points were brought out:

"1) The Englishman believes that be-

—*Continued on page 48a*

Modern MEDICINALS

Physicians will find that these brief resumes of essential information relative to the newer products are so prepared that they may be removed and pasted on standard 3x5" file cards, and filed as illustrated in the adjoining picture, for ready reference.

Calthenamine

7-50

MANUFACTURER: Thomas Leeming and Co., Inc., 155 East 44th St., New York 17, N. Y.

INDICATIONS: Control of pruritus due to ivy or oak poisioning, solare erythema, reaction to drugs such as penicillin, contact (occupational) dermatoses; insect bites and stings; localized neurodermatitis; atopic eczema; pruritus ani et vulvae; and urticaria, acute and chronic.

ACTIVE CONSTITUENTS: Thenylpyramine hydrochloride, 2 per cent; camphorated chloral, 0.30 Gm.; hyoscyamine oleate, 0.04 mg.; menthol, 0.18 Gm.; alcohol, 1.4 cc.; ether, 0.5 cc.; and chloroform, 0.2 cc. per ounce, in a water-soluble Carbowax base.

DOSAGE: As indicated.

HOW SUPPLIED: In 1¼ oz. tubes.

Pyra-Maleate

7-50

MANUFACTURER: VanPelt and Brown, Inc., Richmond, Virginia.

INDICATIONS: In hay fever, vasomotor rhinitis and other allergic conditions.

ACTIVE CONSTITUENTS: Pyranisamine maleate.

DOSAGE: As indicated.

HOW SUPPLIED: In 25 mg. and 50 mg. tablets in bottles of 30, 100 and 1,000.

Lugolcaps

7-50

MANUFACTURER: Burnham Soluble Iodine Company, Auburndale, Massachusetts.

INDICATIONS: Used post-operatively in recurrent hyperthyroidism and in mild hyperthyroidism in which medical management is the treatment of choice.

ACTIVE CONSTITUENT: Each capsule contains 40 mg. of iodine which is the amount present in 0.3 cc., the U.S.P. average dose of Lugol's solution. As in Lugol's solution, part of the iodine is present as free and part as combined iodine. In Lugol's solution the ratio is approximately 40 parts free and 60 parts combined iodine. The capsule contains an equal amount of free and combined iodine. Diglycocoll hydriodide and iodine are used in the capsule in the ratio of two molecules of diglycocoll hydriodide to one of iodine, the formula being $2(CH_2NH_2COOH)_2HI + I_2$.

DOSAGE: As indicated.

HOW SUPPLIED: In bottles of 21 and 100 capsules.

Gentarth

7-50

MANUFACTURER: Raymer Pharmacal Company, Philadelphia 34, Pa.

INDICATIONS: The hyaluronidase-inhibiting action of gentisate ion and the prompt analgesic effect of salicylate ion provide in this product an effective means of treatment of rheumatic diseases, especially arthritis.

ACTIVE CONSTITUENTS: Each orange-colored, salol-coated tablet contains: Sodium gentisate, 100 mg.; Raysal (representing 43 per cent salicylic acid and 3 per cent iodine in a calcium-sodium phosphate buffer salt combination), 325 mg.; succinic acid, 130 mg.

DOSAGE: Two or more tablets three or four times daily.

HOW SUPPLIED: In bottles of 100, 500 and 1000 tablets.

—Continued on page 40a

HAY FEVER

NEURODERMATITIS

CONTACT DERMATITIS

ALLERGIC VASOMOTOR RHINITIS

"DRUG" RASHES OR DERMATOSES DUE TO PENICILLIN OR OTHER DRUGS

URTICARIA, CHRONIC AND ACUTE (PARTICULARLY THE ACUTE)

ATOPIC ECZEMA AND DERMATITIS

COMMON COLD THERAPY

VERNAL CONJUNCTIVITIS

ERYTHEMA MULTIFORME

PRURITUS

A Shield Against Allergic Disorders

DIATRIN* Hydrochloride

'WARNER'

A Superior Antihistaminic of Proved Value[1,2,3]

Effective · Less Toxic · Minimum Side-Effects

PACKAGE INFORMATION: Diatrin* Hydrochloride sugar-coated oral tablets, 50 mg each; bottles of 100 and 1000 tablets.

References

1. Combes, F. C., Zuckerman, R. and Canizares, O: Diatrin Hydrochloride; A New Antihistaminic Agent for the Treatment of Pruritus and Allergic Dermatoses, *Ann. of Allergy*, 7:676, 1949.

2. Kugelmass, I. N.: Antihistaminic Therapy of Allergic Disorders in Infants and Children, *N.Y. State J. M.*, 49:2313, 1949.

3. Combes, F. C., Zuckerman, R. and Canizares, O.: Diatrin Hydrochloride; Clinical and Toxicologic Studies of a New Antihistaminic Agent, *J. Invest. Dermatol.*, 13:139, 1949.

*T. M. Reg. U. S. Pat. Off. **WILLIAM R. WARNER & CO., INC.** New York, St. Louis

new! new! new!

accent on therapeutics!

vi-syneral therapeutic

Vi-Syneral Therapeutic supplies in intensive therapeutic dosage not only the vitamins usually included in the therapeutic type of preparation, but also liver fractions, choline, inositol, folic acid . . . and eight nutritive minerals . . . based upon the original nutritional concepts of Dr. Casimir Funk . . . *that vitamins should be given with minerals* because they are functionally interrelated. The physician and surgeon, therefore, can anticipate results superior to those obtained with less complete formulas.

each dark colored capsule contains:	
Vitamin A (natural)	*25,000 Units*
Vitamin D (natural)	*1,000 Units*
Ascorbic Acid (C)	*150 mg.*
Folic Acid	*1.76 mg.*
Thiamine HCl (B_1)	*15 mg.*
Niacinamide	*150 mg.*
Riboflavin (B_2)	*10 mg.*
Pyridoxine HCl (B_6)	*5 mg.*
Alpha-Tocopherol (E)	*10 mg.*
*Liver Fractions**	*200 mg.*
**B complex factors derived from 7.5 Gm. of liver*	

each light colored capsule contains:	
Choline	*20 mg.*
Inositol	*10 mg.*
d-Calcium Pantothenate	*15 mg.*
Calcium (as 0.31 Gm. di-calc. phosphate)	*160 mg.*
Phosphorus	*132 mg.*
Iron	*15 mg.*
Copper	*1.5 mg.*
Manganese	*1.0 mg.*
Magnesium	*1.0 mg.*
Zinc	*1.0 mg.*
Iodine	*0.1 mg.*

Suggested dose: One dark and one light colored capsule daily.

Prescription packages of 30, 50 and 100 capsules

u. s. vitamin corporation

casimir funk laboratories, inc. (affiliate)

250 E. 43rd St., New York 17, N.Y.

So palatable and so readily digestible is LIVIBRON, nutrient hematinic containing ferrous iron, liver concentrate, and vitamin supplements, that it is tolerated readily by even the most dyspeptic of patients. These are qualities which so eminently adapt it for use in senescence, during pregnancy, and through convalescence following surgery or debilitating illness.

Nutrient tonic and hematinic effects of LIVIBRON specifically offset post-illness asthenia. LIVIBRON may be used advantageously also to meet added vitamin and hematinic requirements of pregnancy and as a general supportive measure in the aged. The pleasant flavor of LIVIBRON assures ready acceptance by children too.

LIVIBRON: supplied in Liquid and Kapseal form. Each 2 teaspoonfuls (or one Kapseal) represents:

Liver Concentrate equivalent of fresh liver	2.5 Gm.
Vitamin B_1 (Thiamine Hydrochloride)	1.25 mg.
Vitamin B_2 (Riboflavin)	0.5 mg.
Ferrous Sulfate	3 gr.
Manganese Citrate	1/16 gr.

PARKE, DAVIS & COMPANY

MEDICAMENTA VERA

—Continued from page 36a

Kondretabs

7-50

MANUFACTURER: The E. L. Patch Company, Stoneham, Massachusetts.

INDICATIONS: A bulk laxative tablet for the control of constipation. Containing two hydrophylic colloids, Kondretabs absorb and retain water. Swell into smooth, velvety bulk which mixes intimately with feces, providing a soft bulk stool.

ACTIVE CONSTITUENTS: Each tablet contains: Irish moss concentrate 0.25 Gm. (3.8 grs.), equivalent to 0.625 Gm. (10 grs.) of Irish moss and methyl cellulose 0.5 Gm. (7.7 grs.).

DOSAGE: One or two tablets, three times a day, with a full glass of water.

HOW SUPPLIED: Bottles of 50 and 100 tablets.

Hepcovite

7-50

MANUFACTURER: Endo Products Inc., 84-40 101st St., Richmond Hill 18, N. Y.

INDICATIONS: Pernicious anemia (uncomplicated or with neurologic complications), nutritional macrocytic anemia due to vitamine B_{12} deficiency, tropical and non-tropical sprue, and certain other cases of macrocytic anemia. Crystalline vitamine B_{12} in children with slow growth resulted in impaired physical development.

ACTIVE CONSTITUENT: Solution of vitamin B_{12} for intramuscular injection.

DOSAGE: As indicated.

HOW SUPPLIED: 15 micrograms per cc. in 10 cc. multiple dose vials and 1 cc. ampul. 30 micrograms per cc. in 5 cc. multiple dose vials.

Abbocillin-DC

7-50

MANUFACTURER: Abbott Laboratories, North Chicago, Ill.

INDICATIONS: For deep intramuscular use only. Abbocillin-DC is indicated in all conditions in which repository penicillin is effective. Clinical trials have shown that single 600,000-unit 1-cc. doses have consistently afforded sustained high blood levels for more than 48 hours.

ACTIVE CONSTITUENTS: 600,000 units (double concentration) of penicillin G procaine in aqueous suspension in a 1-cc. B-D cartridge for use with a B-D disposable cartridge syringe. The suspension is ready for immediate use in office, hospital or home. It does not contain oils or waxes, and flows freely through the needle. It may be stored at room temperature.

DOSAGE: As indicated.

HOW SUPPLIED: Each package contains a disposable plastic syringe with an affixed 20 gauge, 1½ inch stainless steel needle and a glass cartridge-plunger containing a 1-cc. dose of 600,000 units of penicillin G procaine in aqueous suspension. The set is to be used once, then discarded.

Foralamin

7-50

MANUFACTURER: Eaton Laboratories, Inc., Norwich, New York.

INDICATIONS: In such allergic manifestations as symptoms of coryza, pollinosis, allergic rhinitis an conjunctivitis, urticaria, contact dermatoses, atopic eczema, pruritic dermatoses, allergic cephalalgia and food and drug allergy.

ACTIVE CONSTITUENT: N-2-furyl methyl-N-2-pyridyl-N', N'-dimethyl-ethylenediamine fumarate or methafurylene fumarate.

DOSAGE: The average adult dose is one 50 mg. tablet three or four times daily, preferably immediately after meals and on retiring. This may be increased or decreased as experience indicates. For children of 6 years and older, the average dose is 25 mg. two to four times daily. The dose for younger children has not been determined.

HOW SUPPLIED: As 50 mg. scored gray tablets in bottles of 100 and 1000.

—Continued on page 46a

Constipated for a half century; corrected in a matter of days'...

CASE REPORT

A woman, aged 69 years, "complained of obstinate constipation of lifelong duration...She was given 4 tablets of methylcellulose [Cellothyl] before meals and at bedtime and in about a week she began having soft stools and two weeks later she reported that she was having the most satisfactory bowel function that she could ever remember."

CONSTIPATION CORRECTION:

. . . one of the cases reported recently[1] where a "striking change for the better" followed administration of Cellothyl. Cellothyl was also found highly effective in "a large number" of the author's patients who were suffering with severe obstinate constipation: "they had taken quantities or as some of them said 'barrels of laxatives' " without relief until Cellothyl was prescribed.

Physiologic correction—in the colon:

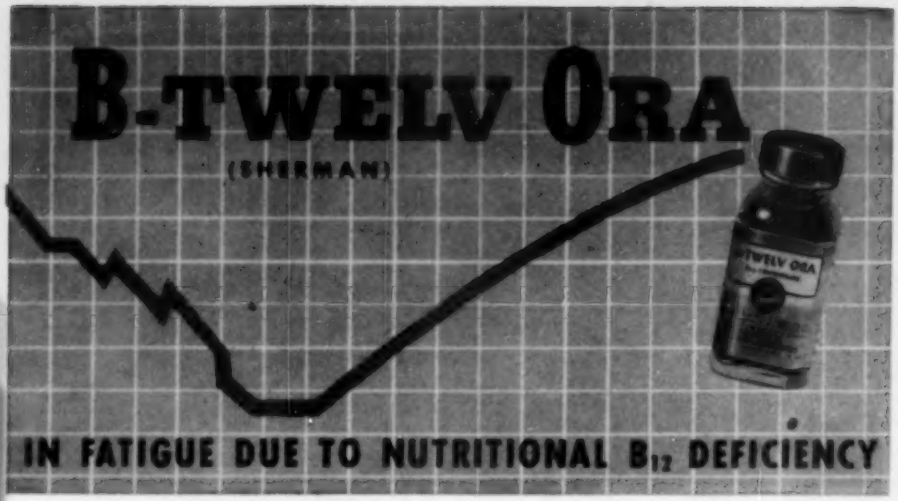
Cellothyl provides bulk where it is needed—in the colon. It passes through the stomach and upper intestines as a fluid and thickens to a smooth gel in the colon to provide bulk for soft, moist, easily passed stools.

The usual starting dose is 3 tablets t.i.d., each dose taken with at least one glass of water. Daily fluid intake must be high, and time must be allowed for correction to begin in an unhurried, physiologic manner. As normal function returns, Cellothyl dosage may be gradually reduced.

1. Bargen, J. A.: Gastroenterology **13**:275 (Oct.) 1949.

Cellothyl®
BRAND OF METHYLCELLULOSE ESPECIALLY PREPARED

CHILCOTT *Laboratories* DIVISION OF The Maltine Company MORRIS PLAINS, NEW JERSEY



VITAMIN B_{12} IN ORAL FORM

● Dietary deficiency of Vitamin B_{12} may result in macrocytic anemia, cytologically indistinguishable from the Addisonian types. Free hydrochloric acid in the gastric juice and response to the extrinsic factor are further clues to nutritional origin.[1]

Incipient deficiency states are more common; retardation of growth, loss of energy and appetite, fatigability are symptoms of early deficiency states, but are non-specific in character.[2]

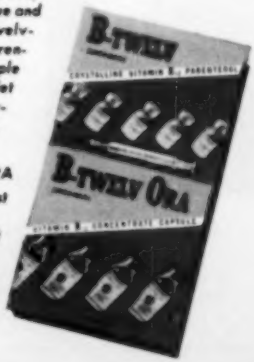
When response to usual measures is unsatisfactory, B-Twelvora may be prescribed. One to three capsules daily (5 to 15 micrograms) is an adequate and safe dosage for incipient B_{12} deficiency.

For prompt response in more severe cases of nutritional deficiency B-Twelv-Crystalline Vitamin B_{12} Parenteral—is recommended.

B-Twelvora is available on prescription at all leading pharmacies.

1. Moore, C. V., Vilter, R., Minnich, V., and Spies, T. D., J. Lab. & Clin. Med. 29:1226 (1944)
2. Youmans, J. B., Nutrition, Its Relation to Deficiency Diseases. Kentucky M. J. 43: 83-88 (1945)

Post yourself on the exceptional therapeutic value and clinical data of B-Twelvora and B-Twelv (Parenteral). Generous sample and this new booklet will be mailed to physicians on request.



SHERMAN LABORATORIES
G. H. Sherman, M. D., Founder
BIOLOGICALS • PHARMACEUTICALS
DETROIT 15, MICHIGAN

B-TWELV ORA
Available list No. 333. Bottles 100 capsules.

A NEW, DRAMATIC THERAPY FOR THE RELIEF OF PAIN AND LESIONS OF

HERPES ZOSTER

ALSO CLINICALLY PROVED FOR THE LIGHTNING PAINS AND ATAXIA OF TABES DORSALIS

DESCRIPTION: Protamide is a sterile, aqueous colloidal solution of a specially processed proteolytic enzyme, for the maximum relief of nerve root pains of Herpes Zoster and Tabes Dorsalis.

CLINICAL RESULTS: Highly gratifying clinical results have been obtained with the use of **Protamide** (Sherman) in the treatment of the extremely resistant herpes syndrome. Pain has been relieved in the great majority of herpes cases within four to forty-eight hours and lesions have healed in ten days or less—regardless of the particular nerve roots involved. Complete clinical data may be obtained by writing for the Protamide literature on Herpes Zoster and a recent reprint on Protamide for Tabes Dorsalis.

DOSAGE: In Herpes Zoster the recommended dosage is 1.3 cc of Protamide intramuscularly each day from two to four days. No contraindications or incompatability have been reported to date. All Protamide is clinically tested for positive results. Can be stored at room temperature without loss of potency.

*REGISTERED U. S. TRADE MARK

SHERMAN LABORATORIES
G. H. Sherman, M. D., Founder
BIOLOGICALS • PHARMACEUTICALS
DETROIT 15, MICHIGAN

Accepted for advertising in the Journal of the AMERICAN MEDICAL ASS'N

When low-sodium dieters complain their food tastes like hay...

Diasal is a new, improved type of salt substitute. It has the crystalline look of salt—virtually *duplicates the taste of salt! Diasal* gives a real salty flavor to flat-tasting, salt-free diet foods. It enables bored dieters to keep on with their diets—*promotes patient cooperation.* *Contains no lithium.*

Diasal is used just like salt, at the table and in cooking.

Constituents: potassium chloride, glutamic acid and inert excipients combined to stimulate food flavors, without bitterness or after-taste. Diasal may be freely prescribed as a diet adjunct in conditions of congestive heart failure, hypertension, arteriosclerosis and edemas of pregnancy.

Available in 2 oz. shakers and 8 oz. bottles.

DIASAL®

restores flavor and taste

no sodium • no lithium

For SAMPLE SHAKERS and low-sodium DIET SHEETS for several patients, write E. Fougera & Co. Inc. 75 Varick St., New York 13, N. Y.

"Premarin" VAGINAL CREAM

...contains conjugated estrogens (equine) which have long been the choice of physicians treating the climacteric. The estrogen content is incorporated in a non-liquefying base which ensures maintenance of consistency at normal body temperature.

"Premarin" Vaginal Cream is standardized in terms of the weight of active water-soluble estrogen content. The potency is declared in milligrams of conjugated estrogens (equine) expressed as sodium estrone sulfate.

"Premarin" Vaginal Cream is valuable alone or as an adjunct to estrogenic therapy by other routes in the treatment of senile vulvovaginitis, pruritus vulvae, and kraurosis vulvae.

For convenience, the combination package is recommended. This package contains a 1½ ounce tube of "Premarin" Vaginal Cream, No. 874 (0.625 mg. per Gm.) together with a specially designed dosage applicator which is calibrated to indicate the quantity of cream administered. The 1½ ounce tube of "Premarin" Vaginal Cream is also supplied without applicator, as a refill.

Also Available: "Premarin" Cream in a non-greasy base, for topical use, is presented in two strengths:
No. 871, 1.25 mg. per Gm., jars containing 1 and 2 ounces;
No. 870, 0.625 mg. per Gm., jars containing 1 and 2 ounces.

Ayerst, McKenna & Harrison Limited
22 East 40th Street, New York 16, N. Y.
2108

—Continued from page 40a

Terramycin

7-50

MANUFACTURER: Charles Pfizer and Co., Inc., Brooklyn, N. Y.
INDICATIONS: In numerous diseases caused by susceptible organisms.
ACTIVE CONSTITUENT: Terramycin.
DOSAGE: As indicated.
HOW SUPPLIED: Vials of 50 mg., 100 mg. and 250 mg. capsules.

Wycillin 600 Suspension

7-50

MANUFACTURER: Wyeth, Inc., 1600 Arch St., Philadelphia 3, Pa.
INDICATIONS: Specifically designed for antisyphilitic treatment in single daily doses, it is recommended also for severe or refractory gonorrhea, pneumonia, streptococcal pharyngitis and other serious penicillin-susceptible infections, when higher dosage is indicated.
ACTIVE CONSTITUENT: Double potency aqueous suspension containing 600,000 units procaine penicillin G per cubic centimeter.
DOSAGE: As indicated.
HOW SUPPLIED: In 1 cc. Tubex, with sterile needle, ready for instant use—no addition or diluent, no sterilization; no waste, only empty vial is discarded after injection.

Chlor-Trimeton Maleate Syrup

7-50

MANUFACTURER: Schering Corporation, Bloomfield, New Jersey.
INDICATIONS: Particularly suited to pediatric use in the treatment of all allergic manifestations where antihistaminic therapy is indicated and as a vehicle for codeine, ammonium chloride, potassium and sodium citrate and sodium salicylate and in combination with elixir terpin hydrate, syrup of cocillana, and tincture of belladonna.
ACTIVE CONSTITUENT: A brilliant green colored, pleasantly flavored antihistaminic syrup containing 2 mg. Chlor-Trimeton per teaspoonful (4 cc.).
DOSAGE: As indicated.
HOW SUPPLIED: Bottles of 16 ounces.

Binat with B_{12}

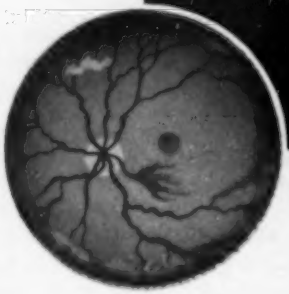
7-50

MANUFACTURER: The National Drug Company, Philadelphia 44, Pa.
INDICATIONS: Oral: Retarded growth in children and general nutritional deficiencies of the vitamin B complex. Injectable: Especially for pernicious anemia and other hyperchromic, macrocytic anemias as well as sprue and other Vitamin B deficiency states; also Laennec's cirrhosis, the neuritites and the psychoses of chronic alcoholism, nonspecific neuritis of pregnancy; trigeminal neuralgia and other forms of neuritis associated with anemia, infections and drugs.
ACTIVE CONSTITUENTS: Oral: Each tablet contains: Whole liver concentrate (1:23) 100 mg. containing a minimum of vitamin B_{12} activity 1 mcg. Vitamin B_{12} concentrate, equivalent to 4 mcg. Total Vitamin B_{12}—5 micrograms; thiamine mononitrate (Vit. B_1), 5 mg.; riboflavin (Vit. B_2), 2 mg.; niacinamide, 50 mg.; calcium pantothenate, 5 mg.; and pyridoxine hydrochloride (Vit. B_6), 1 mg. Injectable: Each cc. contains: Injectable liver (crude), 0.5 cc.; Vitamin B_{12} crystalline, 10 micrograms; niacinamide, 50 mg.; thiamine hydrochloride, 10 mg.; riboflavin, 2 mg.; pyridoxine hydrochloride, 1 mg.; d-Pantothenyl alcohol, 1 mg.; benzyl alcohol, 4 per cent; and phenol, 0.5 per cent.
DOSAGE: Oral: Average adult dose: Prophylactically, one or two tablets daily; therapeutically, two to six tablets daily. Children according to age. Injectable: In pernicious anemia, therapeutic—1 or 2 cc. once or twice weekly, deep intramuscularly; maintenance—1 cc. weekly. In sprue, cirrhosis, multiple vitamin B deficiencies, 5 to 10 cc. in divided doses, as indicated.
HOW SUPPLIED: Oral: In bottles of 24 and 100 tablets. Injectables: In 10 cc. Injectosols.

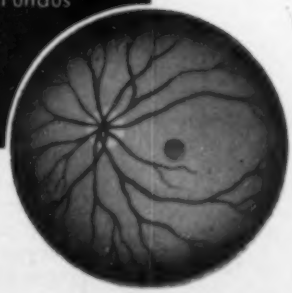
RUTAMINAL*

the protection of **rutin**[1] the action of **aminophylline** the sedation of **phenobarbital** —for use in selected cardiovascular and diabetic conditions in which excessive capillary fragility presents a complicating hazard —bottles of 100 tablets

Ocular Fundus in Degenerative Vascular Disease—Hypertension, Diabetes, Arteriosclerosis —note tortuous blood vessels, areas of exudation, hemorrhagic areas.



Normal Ocular Fundus



[1]In keeping with newer clinical findings, the rutin content of RUTAMINAL has been increased to 60 mg. per tablet (three times the former rutin content) at no increase in cost to the patient.

*RUTAMINAL is the trademark of Schenley Laboratories, Inc. and designates exclusively its brand of tablets containing rutin, aminophylline, and phenobarbital.

schenley laboratories, inc., 350 fifth ave., new york 1, n. y.

LETTERS

continued

from page 34a

cause of Marshall aid the Labor Government has been able to institute the health scheme. But to a man, those interviewed stated they wished that we would not send Marshall aid money, for without this money the government would have to find sounder methods of operation.

"2) Because the greatest percentage of the population comes under the N.H.S. scheme, the stigma of the words 'clinic' and 'panel physician' is eliminated.

"3) Because he contributes, even though in a small way, to the plan, he wants his money's worth whether he needs it or not!

"4) Before N.H.S. the panel physician was available, but the same stigma applies to the term 'panel' in England as applies to 'clinic' in the United States.

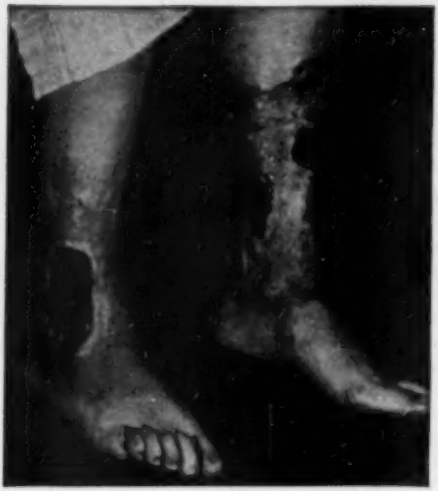
"I returned from England with the thought in mind that the problem in the United States is not that of the physician alone, but concerns each and everyone of us, not because we are in the pharmaceutical industry, but because it concerns the American way of life. Therefore I feel we are under an obligation to ourselves, to our industry and to the medical profession to resist, oppose, and obstruct the passage of any *political* medical bill."

John H. Hinse, General Manager
Fellows Medical Mfg. Co., Inc.

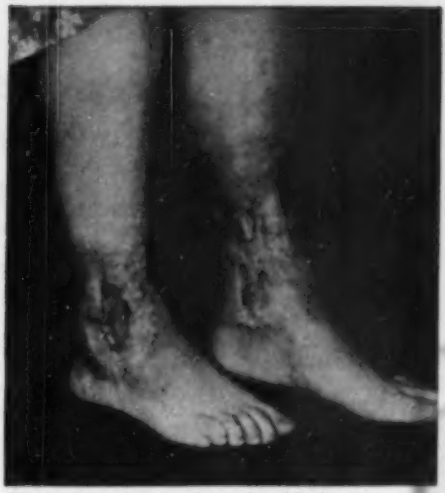
LIKE MT

"I read, study and enjoy your very 'up-to-the-minute' articles on real practical points in the actuality of medicine. Too many Journals get lost in the zest of research medicine, which is of no immediate benefit to the busy general practitioner who must mull over the forever changing and forever increasing armamentarium of our little black bags."

B. Mecklin, M.D.
Watertown, N. Y.



Varicose ulcers of nineteen years' duration. This is one of a series of 50 chronic ulcer cases in which the results of Chloresium Therapy were observed by a leading clinic.



Chloresium therapy brought this improvement in six weeks. Complete healing occurred one month later. Of the fifty cases studied, forty-eight showed marked improvement.

For diabetic and varicose ulcers ... use Chloresium Therapy

Stimulates growth of normal healthy tissue, gives symptomatic relief, deodorizes ... clinically proved.

● In chronic, indolent ulcers, the *problem* is how to aid the healing of tissue which is obviously not able to repair itself. The *answer* is Chloresium, the therapeutic *chlorophyll* preparations. Clinical reports on large series of such cases, which resisted other method of treatment, show that most of them responded rapidly to Chloresium's chlorophyll therapy—and healed completely in relatively short time.

*From the Lahey Clinic Bulletin (Vol. 4, No. 8, April 1946): "The water-soluble chlorophyll containing ointment (*Chloresium*) has now been used at this clinic in more than 50 cases of the more chronic and difficult ulcers . . . (it) apparently excels any of the previously used agents . . . Many patients who had ulcers unhealed from one to eight years obtained complete healing in six to ten weeks."

*From the Guthrie Clinic Bulletin (Vol. 16, No. 1, July 1946): "We have used a water-soluble ointment of chlorophyll (*Chloresium*) in a variety of conditions . . . with splendid results in a vast majority of cases. In a group of chronic ulcers there has been almost universal prompt and early healing."

Try Chloresium on your most resistant case—it is nontoxic, bland, soothing, deodorizing.

*Complete reprints available on request.

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Therapeutic chlorophyll preparations

Solution (Plain); Ointment; Nasal and Aerosol Solutions

Ethically promoted—at leading drugstores

U. S. Pat. 2,141,847—Other Pats. Pend.

FREE—CLINICAL SAMPLES

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I want to try Chloresium Ointment and Chloresium Solution (Plain). Please send clinical samples.

Dr. _____

Address _____

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● Weakened by hunger and pursued by relentless temptations, her already meager powers of resistance are nearly exhausted. At this point, the judicious use of DESOXYN Hydrochloride can avert complete surrender.

With DESOXYN, small doses are sufficient to produce the desired cerebral effect—anorexia, elevation of mood and desire for activity—without producing undesirable side-effects. One 2.5-mg. tablet before breakfast and another about an hour before lunch are usually sufficient. Some patients may require a third tablet about 3:30 in the afternoon. Medication after 4 p.m. may cause insomnia. With small oral doses, no pressor effect has been observed.

Smaller dosage is possible because, milligram for milligram, DESOXYN is more potent than other sympathomimetic amines. DESOXYN also has the advantages of faster action, longer effect.

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(Methamphetamine Hydrochloride, Abbott)

Tablets
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Elixir
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20 mg. per cc.

Ankle Sprain or Ligamentous Fracture of the Ankle

Otho C. Hudson, M.D., F.A.C.S.
Hempstead, N. Y.

There is a large group of cases of "ankle sprains" which are serious. These cases are described from time to time in literature under various titles, such as "tibiofibular diastasis," "tibiofibular sprain," momentary "dislocation of the astragalus," and "ligamentous fractures of the ankle."

For practical purposes, these cases should be classified as a fracture of the ankle with negative x-ray examination. The title "ligamentous fracture of the ankle" is good..

The lesion is serious because lack of treatment for the acute condition leaves a permanently unstable ankle.

The history is a sudden torsion strain on the ankle followed by severe pain. Examination within an hour reveals marked antero-lateral swelling over the lower tibiofibular joint, limitation of flexion and extension of the ankle, no inversion of the ankle, tendency to hold the heel in valgus, spasm of the peroneal tendons, inability to place the heel in varus passively, and an unstable ankle with rocking, laterally, of the astragalus. Routine anteroposterior and lateral roentgenograms are negative. An anteroposterior roentgenogram, made with forced inversion of the foot and varus of the heel, shows the lateral rotation of the astragalus within the ankle mortise.

Examination many hours after the injury reveals exaggeration of the above findings, with heel held fixed in valgus, and with extreme peroneal spasm. There is severe pain when attempt is made to bring the heel to a neutral position with an increase in the peroneal spasm. The diagnosis can be made by the clinical examination.

The treatment is prolonged for all of these cases. Plaster immobilization is necessary.

From the Orthopedic Service of the Nassau Hospital.

We have noticed that immobilization does not relieve the spasm and pain for a long time. The peroneal spasm keeps pulling the foot against the plaster.

We attempted to prevent this post-immobilization pain by section, subcutaneously, of the peroneal tendons. We performed this procedure under local anesthesia a few times with the result that the patient immediately said he was comfortable and with little or no pain.

Our treatment is now subcutaneous tenotomy of the peroneal tendons and immobilization in long leg plaster for six weeks and with a plaster boot for four more weeks. Weight bearing is permitted after four weeks in plaster.

Follow-up studies reveal that the majority of the peroneal tendons function well when the plaster is removed. The ankle is stable and the astragalus cannot be rotated in the mortise.

To our satisfaction, we have proved that "ligamentous ankle fractures" can be made comfortable by a very simple procedure of subcutaneous peroneal tenotomy before immobilization.

We have used this method of treatment for several years with gratifying results. We wish to encourage others to try this method in their practice.

Professional Building

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Observations on Thyroid Disease

Bernard J. Ficarra, M.D., F.I.C.S.
Brooklyn, N. Y.

I

Hyperthyroidism and Neurosis

A purposeful study of the mental attitude of the hyperthyroid patient has revealed an interesting psychic component in these persons. This study culminated in two previous publications. (1,2) One of these distinguished psychosomatic symptoms from borderline hyperthyroidism. The other unfolded major phobias in patients with primary hyperthyroidism. A continuation of this study concerns the presence of neurotic symptoms in hyperthyroid patients; the existence of hyperthyroidism in neurotic individuals; and the relationship between this mental state and organic thyroid disease. Prior to discussing these three categories of patients, thought must be given to the present concept of neuroses; and the abnormal influence of hyperthyroidism on somatic physiology.

A neurosis must be considered as a definite mental illness frequently encountered in modern medicine. Mental illnesses in general must be interpreted as the inability of the individual to mold himself into the environmental pattern. Some serious mental ailments have been labeled as psychoses; milder illnesses with a mental component have been called neuroses or psychoneuroses. In all cases of neurosis the person is made sensitive or has been conditioned by inhibited childhood experiences. The disease becomes manifested by an acute emotional crisis. Anxiety is the root of psychoneurotic reactions. The patient is conscious of his anxiety state, and is confronted by it with a demand for solution. He then attempts to follow some method leading to the solution of his problem. Inadequate handling of the situation results in conversion reaction or conversion hysteria. This conversion of anxiety into disordered functions of the organs or parts of the body is reflected in a train of symptoms which labels the patient a neurotic.

The neurotic symptomatology is limitless. Symptoms are fundamentally characterized by intellectual and emotional reflections, usually given the general label of nervousness. Complaints are identified by the title of nervous stomach, irritable heart, irritable colon, etc. Other symptoms reflect emotionalism in the guise of fears, doubts, anxieties, compulsions and obsessions. An adequate history brings to light many hidden symptoms which formerly were simply called nervousness.

Nervousness is a cardinal symptom in patients with toxic hyperthyroidism. Excessive thyroid activity affects every organ of the body. Hence tachycardia and gastro-intestinal complaints are similar to those symptoms manifested by the neurotic individual. To this symptomatology add phobia, which has been considered a new symptom in hyperthyroidism. (2) Fear being a common attribute of the neurotic patient, the overlapping of symptomatology reflects the contiguous confusion in differentiating neurosis from hyperthyroidism.

Very often the surgeon must assume the responsibility of differentiating the true hyperthyroid patient from the neurotic one. The psychoneurotic person may have witnessed or been a party to a frightening experience. This factor may bring forward symptoms closely paralleling goiter according to the mechanism previously mentioned. The physical examination of such persons may not confirm the history of tremor, sweating and tachycardia. The gland may be normal to inspection and palpation without any audible bruit. The value of the pulse rate and pulse pressure

From the Department of Surgery, St. Peter's Hospital, Brooklyn, New York.

is noteworthy. Psychic factors cause a temporary elevation whereas hyperthyroidism maintains a constantly elevated pulse rate. Usually the toxic thyroid patient is older than the neurotic individual. Emotionalism manifested by spontaneous tears without apparent cause is frequently elicited in true hyperthyroidism. Elevated basal metabolic rate in neurotic patients may occur for many reasons. Technical inaccuracies are frequent. The nervous individual should be informed of the procedure and his cooperation obtained. As a generality it may be stated that cooperation and relaxation are less frequently obtained with psychoneurotics than with hyperthyroid patients. Repetition of the test each morning until a satisfactory technical reading is obtained may reward the observer with a normal basal metabolic recording. Another important differentiating observation is the apparent improvement when these functionally disturbed patients are hospitalized. When these persons are liberated from familial entanglements relief occurs within a few days. Freedom from noxious mental stimuli eradicates the tachycardia and nervous symptoms.[1]

When persons with mental unrest have been convinced of the functional nature of their complaints and are assisted by competent and helpful psychologic suggestions improvement is noted. With the aid of a psychiatrist the so-called hyperthyroid patient undergoes a complete metamorphosis. All patients suspected of mild hyperthyroidism do not fall into this classification. Each individual is a singular problem. There is no one diagnostic pattern applicable to all patients.

Caution is advised against the other extreme of failing to recognize true hyperthyroidism. To brand such a patient a hypochondriac, a malingerer, or a neurotic may terminate deleteriously. It must be remembered that hyperthyroidism is a constitutional disease and as such may display unusual psychic reactions. Although no characteristic psychic reaction is indigenous as regards hyperthyroidism, many of these patients may manifest acute delirium. Some patients with long-standing hyperthyroidism may manifest toxic exhaustive psychosis and other depressive reactions.

The patient with true hyperthyroidism is often overlooked because of the bizarre symptoms occasionally encountered. In classical hyperthyroidism no difficulty arises in making the diagnosis. It is the borderline patient who presents the difficulty and is often mishandled.

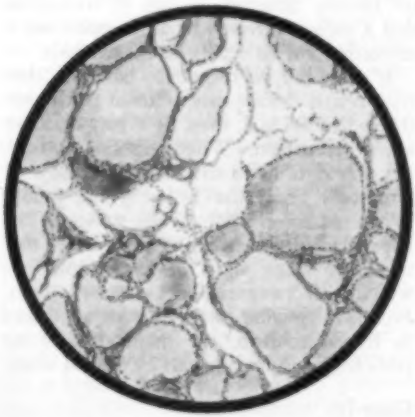

Fig. 1. Microscopic drawing of normal thyroid showing follicles filled with colloid material.

Case I:

An illustration of this type of patient concerns a fifty-two-year-old widow who had a thyroidectomy five years before her present complaints. The present illness, of six months duration, consisted of occasional trembling of arms and legs, intolerance to heat, frequent perspiration and emotional instability characterized by crying without apparent cause. She was sent to a psychiatrist who decided she was not neurotic as previously labeled by several physicians. At the time of her examination the significant findings were a rapid pulse of 120, BMR plus 44, blood pressure 130/70. The left lobe of the thyroid was four to five time enlarged, could readily be seen and when called to the attention of the patient she acknowledged its existence shortly after her previous thyroidectomy.

Her complaints were attributed to a psychoneurosis and she went from doctor to doctor until finally she was referred to a psychiatrist who believed she had organic disease. The diagnosis of hyperthyroidism was made and the patient was prepared for operation. At operation the left lobe of the thyroid was removed. Following surgery her condition markedly improved, she was free from her previous complaints and has now returned to the normal duties of a housewife.

Case II:

A nineteen-year-old woman, unmarried, was treated for six years for gastro-intestinal symptoms characterized by nausea, sense of fullness, occasional diarrhea. In addition to this she was extremely nervous, was very irritable and complained of cardiac palpitation. At the time of examination many of the above symptoms were confirmed plus the fact that she had a phobia which was reflected in the fear of crowds (ochlophobia). Her BMR at this time was plus 25, pulse 106 and blood pressure 140/70. This patient was labeled a neurotic and was sent to a psychiatrist by an internist. It was only after the psychiatrist had adequately studied the individual that the diagnosis of hyperthyroidism was made. She was subsequently operated upon and at the time of this writing, which is three months following operation, she is a changed person without any of the previously mentioned complaints.

Men of medicine and surgery who are conscious of the existence of thyroid disease often become overzealous in their diagnosis. The presence of nervousness, irritability, and palpitation indicts the patient as having hyperthyroidism. This triad of symptoms may result in a thyroidectomy if the surgeon is not alert. Undoubtedly it has been the sad experience of many surgeons to have operated upon patients with true neurosis.

Case III:

A twenty-five-year-old woman employed by the Telephone Company was seen in consultation because of supposed hyperthyroidism. The patient was very nervous

Fig. 2. Microscopic drawing of exopthalmic thyroid showing diffuse hyperplasia and great glandular activity.

and irritable, had palpitation of the heart, and a marked tremor. Her BMR was plus 30. However, after a series of readings it was found to be plus 5. Her pulse was normal, blood pressure was normal. Thyroid was normal to palpation except for the isthmus, which was slightly larger than normal. The clinical picture was not true hyperthyroidism. Finally consultation with a psychiatrist elicted the diagnosis of anxiety neurosis. Thus it transpired that a patient referred by an internist for a thyroidectomy in reality had a neurosis.

It must not be forgotten, however, that true mental disease may occur in the hyperthyroid individual, even as it may occur in any other person. When this situation exists it is difficult to sift the mental class of symptoms from the hyperthyroid group. Where a true mental disease exists in the hyperthyroid patient it is always found that there are many signs of hyperthyroidism which will categorize the disease. Thus, even if the mental complaints are attributed to hyperthroidism, the major underlying pathology will reveal itself by careful study.

Case IV:

A twenty-five-year-old unmarried woman presented the complaint of nervousness, palpitation and fear of crowds. This was

of six months duration. Her pulse was 110, blood pressure was 145/70, BMR was plus 28. Examination of the thyroid revealed an enlarged right lobe and a slightly enlarged left lobe. Diagnosis was: adenomatous goiter with secondary hyperthyroidism. In addition to this complaint, the patient had typical symptoms of anxiety neurosis. She was seen in consultation with a psychiatrist who treated her for neurosis. Both the internist and the psychiatrist prepared her for operation.

When she had been successfully prepared, thyroidectomy was performed followed by an eradication of thyroid symptoms. The psychiatrist then continued to treat her for neurosis. The thyroid symptoms disappeared soon after the operation but the neurotic symptoms manifested themselves as late as four months following surgery.

These cases illustrate several instances of problems in the differential diagnosis between neurosis and hyperthyroidism. The last example demonstrates the presence of both neurosis and hyperthyroidism in the same patient. These cases argue for perspicuity and care in diagosing hyperthyroidism, even as it calls to mind the pitfall in labeling a person a neurotic.

Modern surgery and psychiatry have become necessary supplements to the advancing knowledge of disease. In many cases the combination of thyroidectomy and intensive psychotherapy results in a disappearance of thyroid complaints and neurotic manifestations. This present study emphasizes the need for an adequate history, physical examination and laboratory studies in both neurotic and hyperthyroid patients. The dual cooperation between the surgeon and psychiatrist may save a neurotic patient from a needless thyroidectomy; even as the surgeon's scalpel has eliminated prolonged psychological treatment of patients with hyperthyroidism.

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II

Thiocyanate Myxedema Following Thyroidectomy

The administration of potassium thiocyanate orally for the treatment of hypertension has been advocated by many authors *(1,2,3,4,5,6)*. In addition to lowering the blood pressure this drug has alleviated the distressing headache so frequently associated with hypertension. For this reason some patients may continue to take this drug without proper medical supervision. The recent examination of a post operative thyroid patient has prompted this report concerning a toxic manifestation of thiocyanate.

The patient, Mrs. J.L.N., a forty-four-year-old housewife, was operated upon by me on August 20, 1947. At that time a right hemithyroidectomy was performed for a toxic adenoma. Her blood pressure was 170/100. Her postoperative course was uneventful. In the spring of 1948 she visited her local doctor for headache (This patient lives in upper New York State).

She was given potassium thiocyanate for the relief of hypertension. During the next four months the drug was taken under the supervision of her doctor. Thereafter up to and including the summer of 1949 the drug was taken irregularly without proper supervision. On November 11, 1949 the patient made a special appointment with me because she was "not herself anymore."

At the time of this examination, the patient, who is a very attractive woman, was not recognizable as the same individual of 1947. She had a marked edema of the face, hands and ankles, the skin was dry and scaly, the hair was coarse in appearance. Further examination demonstrated an adenoma of the left lobe of the thyroid, twice the size of the one removed two years previously. Her blood pressure at this time was 190/110.

Further interrogation revealed that the

patient had a toxic reaction from the drug previously which was controlled by an antihistamine drug prescribed by her physician. The patient admitted that she took the thiocyanate irregularly without her physician's knowledge. On one day she would take one tablet and on the second day two tablets. This continued for many months without being checked by her family physician.

Discontinuation of the drug eliminated the signs of myxedema; she has now a large non-toxic adenoma of the left lobe which is to be removed surgically.

Discussion

Many articles have been written concerning the beneficial results of potassium thiocyanate in the treatment of arterial hypertension. There are many contraindications to and side effects of thiocyanate therapy. If the patient is not under constant observation the drug should not be administered. Specifically, blood-thiocyanate determination is the only safe measure against serious toxic manifestations.

The literature contains a report of acute goiter during thiocyanate thereapy for hypertension (7). In this case the large gland regressed and the associated hypothyroid phenomenon subsided under treatment with thyroid extract and iodides.

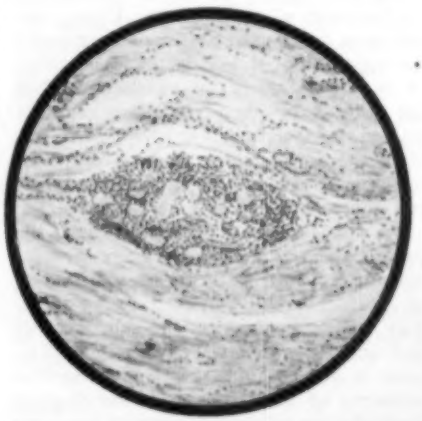

Fig. 3. Microscopic drawing of myxedema thyroid showing only a small island of thyroid tissue infiltrated with round cells remains.

In the patient reported here a previous hemithyroidectomy was performed for an adenoma in 1947.

Exploration of the opposite lobe at the time of operation confirmed the absence of any left-sided adenoma. It is acknowledged that a microscopic adenoma may have been unidentified at operation. Subsequent to her thyroidectomy, the patient was given potassium thiocyanate and continued to take it without proper supervision. She developed a sensitivity to the drug which was controlled by an antihistamine preparation.

In November, 1949, she manifested clinical symptoms of myxedema and a nontoxic adenoma, on the side opposite to her previous hemithyroidectomy, was found. It is believed that all these manifestations, including the thyroid enlargement, are the results of the improper use of potassium thiocyanate.

Summary and Conclusions

1. A report is made of a patient who demonstrated evidence of potassium thiocyanate toxicity.

2. A previous hemithyroidectomy for an adenoma of the right thyroid lobe was performed on this patient in August, 1947.

3. A large non-toxic adenoma is now present on the left side, having been noticed during the period of myxedema while taking potassium thiocyanate (November, 1949).

4. The toxic effects of this drug are emphasized and caution advised in its administration.

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III

Hyperthyroidism In An American Indian (an Anthropological Note)

Interest in thyroid disease never wanes. The clinical and pathological aspects of hyperthyroidism are enthusiastically studied by the surgeon and internist with equal satisfaction. Recently a hyperthyroid patient was treated without any apparent difference between him and many others seen previously. However, during his postoperative stay in the hospital, conversation with his immediate family brought to light that he was a full-blooded American Indian. Never having encountered hyperthyroidism in an American Indian, and not having read of a similar case in the current litrature, I thought this case presentation would interest students of thyroid disease.

Case Report

The patient, M. S., a 55-year-old ironworker, was seen for the first time in November, 1947. At that time he was under treatment by his family physician for hyperthyroidism. He had the classical symptoms: nervousness, weight loss, palpitation, tremor, exophthalmos and signs of cardiac insufficiency. He was classified as a thyrocardiac. A BMR was taken which was plus 35. He had never been ill until the onset of this illness, which was of two months duration, according to his history.

After an adequate preoperative regimen he was subjected to subtotal thyroidectomy. His postoperative course was uneventful and he was discharged from the hospital.

Discussion

During the patient's postoperative period his immediate family was seen for the first time. Their general appearance was similar to that of any other Americans; however, close observation revealed characteristics of the red race. This led to questioning and a subsequent lesson on American Indians.

The patient informed me that he was a full-blooded American Indian of the Mohawk tribe. The Mohawks were members of the Iroquois League. The strongest of all the Indian groups living east of the Mississippi River were the five tribes composing the Iroquoian League or Five Nations. These tribes, the Mohawks, Oneidas, Onondagas, Cayugas and Senecas, held the land from Lake Huron to the Atlantic Coast, and south through New York and Pennsylvania. Today the Iroquois live on reservations in New York State and Ontario. Their population is about 17,000.

The father of the patient under discussion lived on a New York reservation. The son left the reservation as a child and lived in the city. He settled in Brooklyn where there is a small colony of Indians. This colony is located in the less desirable part of the Borough. Most of the men in this colony earn their living as ironworkers.

Many of these men or their fathers before them adopted names of flowers, plants or trees. Others are called after parts of a tree as Branch, Leaf, etc. Our patient was named after a part of a plant.

Recently, according to a follow-up letter, it has been learned that this patient has developed pleural effusion. The etiology probably is tuberculosis. This disease results in an extremely high mortality in the red race.

Summary

A report is given on an American Indian who developed primary hyperthyroidism. This clinical entity is infrequently seen in American Indians. For this reason the case is worthy of recording.

The degree of these Indians' integration into our civilization affects the incidence of such ailments as hyperthyroidism and tuberculosis in this segment of our population, the ailments becoming a rough measure of the integration and a matter of anthropological interest.

567 First Street

SPECIAL ARTICLE

The Newer Antibiotics Having Wide Antibacterial Spectra

This summarization attempts to cover the essential therapeutic information on the subject and is designed as a time-saving refresher for the busy practitioner.

Reprints available*

Recently there has been added to the chemotherapeutic agents used in therapy three new antibiotics; chloramphenicol, aureomycin and terramycin. Each one of these has been shown to have a broad antibacterial spectrum. New reports of additional conditions in which they are useful appear almost daily.

Chloramphenicol

Chloramphenicol was first isolated from *Streptomyces venezuelae,* an actinomycete found in a sample of soil in Venezuela by Burkholder of Yale University.[1,2] Later a similar strain was found in a compost pile in Illinois.[3] This antibiotic is unusual not only in its antibacterial spectrum but in the fact that it may be prepared synthetically on a practical basis. The chemical structure of chloramphenicol is rather simple, making its synthesis relatively easy in contrast to some of the other antibiotic agents.

I. Properties

Chloramphenicol chemically is D-threo-1-paranitrophenyl-2-dichloroacetamide-1,3-propanediol and it occurs in elongated tablets or needles. It is relatively stable in that it retains 100 per cent of its activity in a pH of 0.4 to 9.56. It is unaffected by boiling in distilled water for a number of hours.[2a] Solutions of 0.25 per cent in distilled water may be stored under refrigeration for months for use as standards in assay work. Those containing less than 1.0 mg./ml. deteriorate in a few days to a week under refrigeration. At a pH of 10.82 only 13 per cent of its activity is present after the solution is kept at 25° C. for 24 hours. It has a bitter taste and is not very soluble in water. For this reason, when it is necessary to administer it parenterally, propylene glycol is the vehicle used.

II. Experimental Studies

Experimental studies revealed that this new compound possesses some effect in the treatment of epidemic typhus, whooping cough, Friedländer's pneumonia, typhoid fever, undulant fever, urinary tract infections and some bacillary dysenteries. In broth cultures, chloramphenicol was found to be more active against gram-positive and acid-fast species. When compared with streptomycin, it was found to be only one-tenth as active against streptomycin-sensitive strains of *Mycobacterium tuberculosis.* Against tested gram-negative species, chloramphenicol was 7 to 36 times as active as penicillin but much less active against

*From the Editorial Research Department of the MEDICAL TIMES, 67 Wall Street, New York 5, N. Y. Permanent library binders, sufficient to hold 24 different "refresher" reprints, sent postpaid, $2.50.

Staphylococcus aureus. Penicillin, in concentration of 100 units per cc., was inactive against *Borrelia recurrentis* but chloramphenicol appeared to have remarkable activity. Protozoa are only very slightly affected by this new agent. Studies of mobile amebae in *E. histolytica* cultures showed that chloramphenicol caused a decrease in number but this was attributed to inhibition of the associated mixed bacterial flora. Chloramphenicol has no effect on fungi as shown by *in vitro* tests.

The concentrations of chloramphenicol (in mg./ml.) necessary for inhibiting various organisms are as follows: *Alcaligenes fecalis*, 1.0; *Bacillus anthracis*, 1.0-5.0; *Brucella abortus*, 2.5-10; *Clostridia* (genus), 500; *Corynebacterium diphtheriae*, 0.5; *Diplococcus pneumoniae*, 1.0-2.5; *Escherichia coli*, 2.5; *Hemophilus influenzae*, 3.6; *Hemophilus pertussis*, 0.2; *Klebsiella pneumoniae*, 0.5-2.5; *Malleomyces mallei*, 40; *Mycobacterium tuberculosis*, 6-12; *Neisseria meningitidis*, 2.5; *Pasteurella* (genus), 0.2-2.5; *Proteus* (genus), 1-25; *Pseudomonas* (genus), 10-100; *Salmonella enteritidis*, 0.7-2.5; *Salmonella paratyphi*, 0.7; *Salmonella schottmuelleri*, 0.5-2.5; *Salmonella typhosa*, 1-5.0; *Shigella dysenteriae*, 0.7; *Shigella paradysenteriae*, 0.5-2.5; *Shigella sonnei*, 2.5-5.0; *Streptococcus pyogenes* (hemolyticus), 0.7-2.5; and *Vibrio comma*, 1.0.[3b]

Animal studies were next made and it was found that chloramphenicol had considerable therapeutic effect on experimental rickettsial infections. Tests with chick embryos infected with *Rickettsia prowazeki* revealed that gram for gram this new agent was more effective against this organism than any other agent tested. Experimental avian malaria and rabbit syphilis were not affected.[4] Only moderate dosage was necessary to elicit response against *Vibrio comma* and *Hemophilus pertussis*.

Summarized, the inhibitory effect on the rickettsiae involved in epidemic typhus, murine typhus, scrub typhus, Rocky Mountain spotted fever, rickettsialpox and Q fever was marked.[2, 4a, 4b] Marked inhibition was also noted on the virus infections of lymphogranuloma venereum and psittacosis induced in laboratory animals.[4, 4a] No inhibition was noted in the following conditions: Variola-vaccinia, influenza A, A[1] and B, mumps, lymphocytic choriomeningitis, eastern equine encephalomyelitis, western equine encephalomyelitis, St. Louis encephalitis, Japanese encephalitis, rabies, poliomyelitis (Lansing, Yale-SE), mouse encephalomyelitis, distemper, Newcastle disease, chick bronchitis, and laryngotracheitis.[2b, 4a, 5]

Resistant variants of previously sensitive organisms to chloramphenicol have been produced *in vitro*.[2b] Thus far no resistant strains of rickettsiae have been developed.[4b] However, in the therapy of scrub typhus and typhoid fever in humans there is no evidence of any resistant strains developing so that it is considered to be of minor significance.[6-9]

III. Pharmacology

Tolerance studies of chloramphenicol in white mice revealed that the maximum tolerated dose of this drug given intravenously is 200 mg./Kg.[5]; the LD_{50} is about 245 mg./Kg. When orally administered in acacia suspension a dosage of 1 Gm./Kg. caused a depression in some animals but they recovered from this in less than 24 hours. After 1.25 Gm./Kg. tremors and prostration occurred followed by recovery.[5] When the antibiotic was given subcutaneously with propylene glycol as a vehicle a slight depression of weight gain was observed over a period of 15 days following a dosage of 100 mg./Kg. in 2 divided daily doses. Tests with rabbits showed that 100 mg./Kg. daily given subcutaneously in 2 divided doses were tolerated for 8 days.

Experiments with 72 to 88 mg./Kg. dosage in dogs revealed no significant changes in total white cell or differential counts, blood non-protein nitrogen, blood sugar or bromsulfalein liver function tests. No alterations in behavior which could be traced to the drug were observed. Urinalysis showed no albumin or reducing sugar and the pH and specific gravity were normal.[5]

From these animal experiments it was concluded that chloramphenicol is either

inactivated or fairly rapidly excreted in animals.

IV. Human Studies

Tolerance studies in normal human subjects were made, also giving an initial dose of 1 Gm. followed by 0.2 Gm. every 4 hours (except at 4 A.M.) for a period of 10 days. Maximum blood levels (approximately 6 μg. per cc.) were attained in 2 hours. They then declined steadily until none could be detected after 8 hours. The levels in the urine also reached a peak (200 μg. per cc.) in 2 hours and then steadily declined to 50 μg. per cc. where they remained for 10 days. The blood and urine showed no abnormalities.[10]

In a second test the subjects were given an initial dose of 2 Gm. followed by one 0.5 Gm. dose 8 hours later. This dosage provided relatively high blood levels and appreciable quantities in the urine within 30 minutes after administration. After two hours the blood levels exceeded 10 μg. per cc. and at 8 hours, 5 μg. per cc. The urine levels were 670 and 380 μg. per cc. after 2 hours and then dropped to 10 μg. per cc. Tests revealed that approximately 10 per cent of the daily dose could be recovered in active form.[10] It was thought that the nitrobenzene radical in the structure might harm the hemopoietic system but no significant changes in the red or white blood cells have been observed thus far. No evidence of renal or hepatic involvement has developed either.[6-9]

In some patients given large single doses a transient mild euphoria has been reported. Other side reactions have included mild gastrointestinal disturbances such as moderate gaseous distention and a minor change in the consistency of the stools for a few days. Glossitis has been reported in some patients given the drug for a week or longer. This condition was characterized by tenderness, hyperemia and marked prominence of the lingual papillae. When therapy was discontinued this condition continued for a few days. Pruritus ani was reported in a few cases when the drug was given over a long period of time.[11]

These reactions, however, are not considered serious. Thus far no serious symptoms or signs of toxicity have been reported. With more extensive use of chloramphenicol it is important that any untoward reactions be watched for carefully.

V. Indications

The indications for chloramphenicol are numerous and include the following diseases: brucellosis, bacillary urinary infections, primary atypical pneumonia, typhoid fever, epidemic typhus fever, scrub typhus, murine typhus, Rocky Mountain spotted fever, tularemia, whooping cough, influenzal meningitis, gonorrhea, cholera, plague, bacillary dysentery, melioidosis,[13a] lymphogranuloma venereum, granuloma inguinale, psittacosis, herpes zoster, infectious mononucleosis, pertussis, and relapsing fever. In some cases of syphilis good results have been obtained so that further studies are being conducted. It is possible also that chloramphenicol may have some value in tuberculosis.

A. Brucellosis

In the therapy of active undulant fever the dosage recommended is an initial dose of 60 mg./Kg. followed by 0.25 Gm. every 3 hours for at least 7 days of normal temperature. In 6 patients with active undulant fever treated with chloramphenicol it was found that the fever lasted for only 2.4 days (average) and the drug was given for 8.5 days.

In another series of 9 patients, 6 were suffering from an initial attack and 3 from a relapse which began in 2 to 5 months after the original illness had been controlled by streptomycin and sulfadiazine combined. The blood cultures revealed that 4 were infected with *Brucella abortus*, 2 with *Br. suis* and one with *Br. melitensis*. The other 2 cases were diagnosed by means of agglutination tests. After therapy with chloramphenicol was begun the fever subsided on an average of 2.7 days. The initial dose was approximately 50 mg./Kg. of body weight followed by doses of 0.25 Gm. every 3 hours until the temperature was restored to normal and for no less than 5 days after that. A follow up of the patients for 6 to 9 months revealed a relapse in one within 30 days after therapy

was stopped. Resumption of therapy again reduced the fever.[12, 13]

In a group of 135 patients with brucellosis 110 were given aureomycin and 25 chloramphenicol. Because diagnosis of only one case was proven by culture methods the results are not considered as too definite.[14] Similar results have been achieved with aureomycin so that no statements can be made as to the superiority of one over the other in this condition.[12, 13]

Chloramphenicol also may be of some value in chronic undulant fever but prolonged therapy would probably be necessary. The evaluation of the drug in this condition may be more difficult.

B. Bacillary Urinary Infections

Although it is not definitely established whether bacilli are primary or secondary invaders in bacillary urinary infections the incidence of such infections is relatively great. Because chloramphenicol is found in greater quantities in the urine than in the blood and it is inhibitory to a number of the organisms causing urinary tract infections it was tested for its value in these infections. Twenty-five patients with various types of infections were selected.

After oral administration of 2 to 3 Gm. divided into 2 to 4 parts daily the urine was freed of bacteria in 1 to 3 days. The length of time in which therapy was necessary was somewhat variable because the basic cause for the infection was not always known or could not be eliminated. Patients with infections caused by *E. coli, Aerobacter aerogenes, Pseudomonas aeruginosa, Klebsiella, Salmonella schottmuelleri* and *B. proteus* responded favorably to therapy with chloramphenicol.

It is recommended that, after the initial dose, a dosage of 0.25 Gm. 3 or 4 times a day should be given for 5 to 7 days after the principal invader has been eliminated from the urine or until the focus has been eradicated by operation.

Doses of 1.0 to 3.0 Gm. daily were found to free the urine of bacteria within a day or two.[15, 15a, 15b] In cases with active urinary pathology, malignancy, calculi, urine retention, various anatomical anomalies and other related conditions it may be impossible to maintain a sterile urine since cocci have been found to appear after the bacillary infection has been eradicated. In order to control the infection permanently, any interference with the urinary flow must be corrected. If the original major infection recurs another course of chloramphenicol is indicated.

In the therapy of salmonellosis chloramphenicol has shown considerable promise. In two carriers who had resisted all other therapy negative stool cultures were obtained in 10-14 days of therapy with 125 mg. every 4 hours.[15c] Given to 9 infants with salmonella enteritis chloramphenicol also produced improvement.[15d] It was administered in doses of 110-480 mg./Kg. daily for 14 days with no signs of toxicity.

C. Typhoid Fever

In Kuala Lumpur there frequently is found a severe type of typhoid fever. Consequently chloramphenicol was tested on 10 selected cases in this area.[7] Eight control cases also were selected. The dosage used was 50 mg./Kg. initially, followed by 0.25 Gm. every 2 hours until the temperature resumed the normal level. Therapy with the same dose every 3 or 4 hours was then continued for 5 days. The treatment period averaged 8.1 days and the total dosage to any one patient was 19.1 Gm. No toxic effects were observed. After therapy was begun the fever usually disappeared in 3.5 days (average). Since this initial trial additional clinical tests have confirmed the results[7, 8, 10] and the dosage described is recommended. Because of the rapid action of the antibiotic it was found that the fever receded before the intestinal lesions were healed so that hemorrhage and perforation occasionally developed during or immediately following defervescence. However, the patients all recovered.[8]

In a study of the two relapses of the first 10 cases treated it was found that the length of period of therapy affected the incidence of relapse.[16] In a group of 13 patients given the antibiotic for 8 days or less (average of 6.9 days) seven had relapses whereas in a group of 19 patients given the antibiotic for 9 to 14 days (aver-

age of 11.2 days) there were no relapses. Continuation of therapy for 14 to 23 days also resulted in no relapses in 12 patients. As a result of these findings the total dosage recommended is 25 to 30 Gm. in 10 to 12 days given in an initial dose of 3.0 Gm. followed by daily doses of 3.0 Gm. (divided) until the fever is gone. For the following 8 to 10 days the daily dose should be 2.0 Gm.

In most cases examination of the blood revealed no *S. typhosa* organisms within a few hours after beginning therapy. Except for the relapse cases the blood remained sterile. Approximately 50 per cent had the organism in the feces after therapy was begun but after it was discontinued no organisms were found in most cases. The organism did recur in the stools of those who had relapses.[9] Further studies have confirmed the value of chloramphenicol in treating typhoid fever.[17-17b]

A study of the carrier state of typhoid fever revealed that it is not eradicated by therapy with chloramphenicol.[9, 17]

D. Gonorrhea

A recent report has shown that chloramphenicol effectively cured 30 of 32 cases of gonorrhea.[18] Some patients were given doses of 1 to 1.5 Gm. and others 3.0 to 3.5 Gm. Only 4 relapses were observed. In 2 of these the patients were inebriated and it is believed that alcoholism may be a disturbing factor. One other case which relapsed 28 days after therapy was believed due to reinfection. In the fourth case the patient was cured in 36 hours after being given 1.0 Gm. of the drug but relapsed in 14 days. Additional administration of one dose of 3.0 Gm. to these relapsed patients produced good response.

Response to chloramphenicol was noted by these and, in an additional group of patients, the fact that dysuria disappeared within 36 hours and the discharge within 49 hours. This was determined by the absence of exudate on stripping. Examination of smears made of the discharge revealed that within 24 hours the gonococci were eliminated in all but a few cases and in those patients who still showed presence of gonococci in 48 hours leukocytes were usually absent from the discharge.[19, 20] Other studies have produced similar results.[20a]

E. Syphilis

In rabbits infected with syphilis chloramphenicol appeared to have only a limited effect.[21] This also was substantiated in 2 humans having syphilitic chancres. The spirochetes disappeared and the primary lesion healed following several days of oral administration of chloramphenicol. But about a month later both patients had recurrences of the lesions at the original sites. From these experiments it was believed that chloramphenicol might not have any inhibitory effect on syphilis while in the incubation stage.[20]

However, because it is less effective against *Treponema pallidum* than penicillin it does not mask the signs of the infection when used in treating gonorrhea. In another report of its use in early syphilis it appeared to promote healing by a different mechanism than penicillin. Penicillin produces initial healing at the periphery of a lesion in contrast to chloramphenicol which initiates it from the base of the lesion. This is especially noticeable in the large ulcers of benign tertian syphilis of the skin. The recommended dose is 30 mg. per Kg. of body weight daily divided into 6 doses and given at 4 hour intervals. In a group of 24 patients treated thus initial healing of the lesions was observed within 24 hours. In some patients, particularly where the lesion was located in the urethra and there was a constant flow of urine over it, healing was delayed slightly.[22]

Further studies on the effect of chloramphenicol in syphilis are being conducted. Since the established methods of therapy are relatively efficient the investigations are limited to certain specialized centers where it can be evaluated adequately.[19, 22a, 22b]

F. Primary Atypical Pneumonia

Chloramphenicol also has been used in the therapy of a few cases of primary atypical pneumonia associated with the development of cold agglutinins. It was administered in doses of 0.5 Gm. every 2 or 3 hours until 3 Gm. were given when the

same dosage was given 4 times a day. Within 36 to 48 hours the temperature was reduced to the normal level. In order to prevent relapse, therapy should be continued for 3 to 5 days after the temperature becomes normal.

Further work is necessary in this condition since atypical pneumonia is a clinical syndrome with a number of etiologic agents but the agent involved in the cold agglutination phenomenon has not been transmitted to animals.[19,23,24,25]

R. burneti and the psittacosis virus also produce pulmonary diseases which cannot be distinguished from primary atypical pneumonia in which the cause is unknown. However, chloramphenicol is effective against these organisms so that differential diagnosis is important.[19]

G. Miscellaneous Infections

Chloramphenicol has also shown value in treating the virus infection, lymphogranuloma venereum. Granuloma inguinale also has shown response to this antibiotic. A series of 5 patients treated with a dosage of 25 Gm. over a period of 5 to 10 days showed improvement. Within a few days after the beginning of therapy there were no Donovan bodies in the lesions.[26]

Several cases of paratyphoid A and B fever have been treated successfully with chloramphenicol. The recommended dose is 50 mg./Kg. initially followed by 0.25 Gm. every 2 hours and later every 3 or 4 hours.[26a-g]

Relapsing fever, caused by organisms similar to those in syphilis, may possibly be affected by chloramphenicol. This requires further investigation.

Surgical infections have been successfully treated with chloramphenicol also.[27] Pelvic peritonitis and cholangitis have responded favorably.[27a]

In severe diarrhea in infants due to unknown cause and which has resisted other therapy chloramphenicol has shown value in doses of 0.05 Gm./Kg. for 7-10 days.[27b]

One case of fulminating otogenic meningitis due to *E. coli* has been reported as successfully treated with chloramphenicol in 5 days with no toxic effects.[27c]

Immediate and progressive recovery has been reported following administration of the antibiotic in 1 case of acute otitis media due to *K. pneumoniae*.[27d]

Two cases of infectious mononucleosis have been treated successfully with chloramphenicol. One was an adult with a relapsing case. The dosage used was 50 mg./Kg. given in 3 parts initially and then 0.5 Gm. every 4 hours for 8 days. The other case was an 8-year-old boy who showed marked improvement from the beginning of therapy with 30 mg./Kg. every 6 hours for 3 days. A relapse occurred but was relieved by further administration of the drug.[27e, 27f]

Relief from pain occurred in a patient with herpes zoster within four hours after the first dose of chloramphenicol. Lesions healed rapidly and the patient became asymptomatic on a dosage schedule of 0.50 Gm. initially, followed by 0.25 every four hours until 6.0 Gm. had been given.[27g]

Favorable results have been obtained with chloramphenicol in the therapy of pertussis as well. In one case a 5½ months old girl was given the drug in doses of 0.25 Gm. every 4 hours in powder form through an esophageal catheter a half hour before each four-hour feeding. Seven doses were given and improvement was noticeable within 12 hours of the first dose. The effect was very startling. However, there was some colic and diarrhea and recurrence of coughing attacks. It is recommended that smaller doses over a longer period of time might eliminate this.[27h] Similar results were obtained by other workers.[27i] In the epidemic in Bolivia chloramphenicol was given to 50 of the most severely ill patients. Fever, present in all patients under 5 years of age and in most older patients, disappeared during the second day of treatment, and the number of paroxysms was definitely decreased on the third day and disappeared after three to six days of treatment. The drug was given orally, rectally, and intravenously (dissolved in propylene glycol). Oral dosage was 0.25 Gm. initially, then 0.25 Gm. two to four times daily for a total averaging 2.5 Gm. Results of intravenous and rectal dosage were equal to those ob-

tained by the oral route.[97]

Use of chloramphenicol with variable results has also been reported in numerous other infections such as are listed in the beginning of this review.

H. Rickettsial Disease

1. Typhus fever (epidemic and murine)

Chloramphenicol was first tested for its effectiveness in therapy of epidemic typhus fever.[20]. Clinical trials confirmed the encouraging results which had been found in preliminary experiments.[5, 16] In 2 cases of epidemic typhus given the drug either orally or intravenously the temperature and pulse returned to normal within 24 to 54 hours and the symptoms were relieved in 36 to 72 hours. The daily dosage given orally was 1.0 to 3.5 Gm. Some patients also were given 0.3 to 1.2 Gm. intravenously as well. No signs of toxicity or intolerence were observed. The patients were checked for several months after therapy.

Further clinical studies were also made on 5 typhus fever patients in 4 of whom *Rickettsia prowazeki* (epidemic) and in 1 of whom *R. mooseri* (endemic or murine) was the organism. One of the 4 and the latter patient were young children.[20, 20, 20a]

From the experiences of the various clinical trials conducted the dosage recommended now is 60 mg./Kg. (3-4 Gm.) initially followed by 0.25 Gm. every 5 hours for 24 hours or until the fever is eliminated. In young children it may be necessary to give a slightly greater dose than derived from the proportional weight-dose ratio. In some cases it was found that a single oral dose of 3.0 to 4.0 Gm. was sufficient to control the disease.

2. Scrub typhus

Scrub typhus or Tsutsugamushi is caused by rickettsiae called *R. tsutsugamushi* and *R. orientalis* which are borne by mites. This disease is generally found in parts of the Japanese Archipelago and in Southeastern Asia (particularly Malaya). Twenty-five such patients were first treated with chloramphenicol in Kuala Lumpur.[9] An initial dose of 50 mg./Kg. was given followed by 0.2 to 0.3 Gm. every 2-4 hours. In the beginning therapy was continued for a minimum of 12 days and a total dosage of 8-15 Gm. after the symptoms began but these were reduced and a group of 7 patients was given a total of 6 Gm. in a 24-hour period. These patients showed just as much improvement as the ones given the longer course. The dosage now recommended is 60 mg./Kg. initially followed by 0.25 Gm. every 3 hours for 7 doses or until the fever is gone.

For prophylaxis the dosage recommended is 1.0 Gm. daily or 4.0 Gm. weekly. When continued for only 2 weeks after exposure scrub typhus developed approximately 1 week after the last prophylactic dose.[31] When the dosage was continued for 4 weeks the disease did not develop. [17a, 19, 32] These results lead to the theory that chloramphenicol is rickettsiostatic rather than rickettsiocidal and that it must be given long enough for an immunity to develop.[19]

3. Rocky Mountain Spotted Fever

Although Rocky Mountain spotted fever is found in the Rocky Mountain area there is also a form of it endemic in Maryland. In the former area the vector is the wood-tick and in the latter area the dog-tick is responsible. In either type the etiologic agent is *Dermacentroxenus rickettsi*.

Fifteen cases of the eastern type were given 75 mg./Kg. in 2 or 3 parts at 1 hour intervals initially, followed by 0.25 Gm. (children under 16 years) every 3 hours. Patients over 16 years of age were given 0.5 Gm.[17a] In the first 24 hours steady improvement was shown but on the second day the symptoms such as headache, mental dullness and others were definitely less intense. The temperature dropped to normal within 76 hours. No relapses were observed even though therapy was stopped 24 hours after the patients became afebrile. Very few if any signs of toxicity were observed. One case of vomiting was attributed to a psychosomatic origin.

The dosage recommended in treating this condition is 60 mg./Kg. initially followed by 0.25 Gm. every 3 hours until the temperature is normal for 48 hours. Ad-

ditional reports have confirmed the evidence.[33, 34]

I. Tularemia

Although the experimental mouse infections were not affected to any striking extent by chloramphenicol a recent report shows that this antibiotic is of value in treating human cases of tularemia. Given to 6 patients in a dosage of 3.0 Gm. initially followed by 0.5 Gm. every 4 hours for 5 to 7 days striking results were produced. The temperature returned to normal in less than 2 days and the headache disappeared in 3 days. Strength and appetite returned in 3 days. Pulmonary manifestations were relieved in 2 days in the 2 patients having them. In 3 patients with the ulceroglandular form the primary lesions healed rapidly and the involved lymph nodes did not progress to suppuration. To prevent relapses it is recommended that 3 more days of drug therapy be given after a rest of 2 days following the initial courses of treatment.[34, 35]

Aureomycin

From another species of the actinomycetes still another antibiotic has been isolated. Named *Streptomyces aureofaciens* this organism yields aureomycin. Discovered by Duggar this antibiotic has a wide antibacterial spectrum.[36]

I. Properties

Aureomycin is a weakly basic compound containing both nitrogen and non-ionic chlorine. The crystalline free base is soluble in water to the extent of 0.5-0.6 mg./ml. at 25°C. It is very soluble in the cellosolves, dioxane and carbitol; slightly soluble in methanol, ethanol, butanol, acetone, ethyl acetate, and benzene; insoluble in ether and petroleum ether; very soluble in aqueous solution above pH 8.5. The hydrochloride is more soluble in water having an approximate solubility of 14 mg./ml. at 25°C. The pH of the aqueous solution is 2.8 to 2.9.[37]

Crystalline aureomycin hydrochloride is stable when it is dry. The potency is maintained for many months at 20-25°C.[38] When in solution it deteriorates rather rapidly dependent upon the pH, temperature and type of solvent. No measurable loss of potency has been demonstrated for 25 days in an unbuffered solution in distilled water at a pH of 2.9 and stored at approximately 4°C.[39] Other workers reported that aureomycin is quite unstable at a neutral or alkaline pH even when stored at 4°C. As the temperature is raised the instability increases in direct proportion. At a pH of approximately 7.0 almost 60 per cent of the potency is lost in 18 hours at 37°C. and 75 per cent is lost in 4 hours at 56°C. The initial bacteriostatic potency is considerably less when the reaction is alkaline rather than acid. Various ingredients of the culture media also affect the potency.[40-43]

II. Experimental Studies

In vitro tests of aureomycin indicate that it is effective against both gram negative and gram positive bacteria. However, higher concentrations are necessary to produce bacteriostasis with gram positive organisms than are required of penicillin. Against gram negative bacteria it has approximately the same or slightly less activity than streptomycin.[40]

To inhibit certain strains of *S. hemolyticus, S. faecalis, D. pneumoniae* and *S. aureus* a concentration of 1.25 μg. or less per ml. was required. For *E. coli, A. aerogenes* and *K. pneumoniae* a concentration of 1.25 to 5.0 μg. per ml. was necessary.[43] Other workers also reported bacteriostatic concentrations as low as 1.0 μg. per ml. for hemolytic streptococci, pneumococci, gonococci and meningococci. Concentrations of 1.0-2.0μg. per ml. were inhibitory to most strains of *Staphylococcus aureus* but a few required as much as 12.5 μg. per ml. Concentrations of 3.1 to 25.0 μg. per ml. were required in tests with gram negative organisms such as the typhoid bacillus and other members of the Salmonella group. Moderate or marked resistance is shown by almost all strains of *Proteus* and *Ps. aeruginosa* since they required concentrations of 4.0 to 250 μg. per ml.[44] Occasionally a strain is found which is very sensitive, requiring only 0.0125-0.4 μg. per ml.[45] *In vitro* tests

with *S. faecalis* have shown that this is more sensitive to aureomycin than to penicillin.

Aureomycin is also effective against the Brucella organisms. Concentrations of 0.25 to 0.5 μg. per ml. completely inhibited *Brucella suis* and 0.25 to 2.0 μg. per ml. completely inhibited *Br. abortus*.[46] These findings were confirmed by other investigators who also found that aureomycin possessed activity against *Br. melitensis* as well.[47]

Tests for the tuberculostatic activity of this antibiotic revealed that concentrations of 2.5 to 40.0 μg. per ml. inhibited a standard strain of *M. tuberculosis*, H37Rv, in certain types of fluid media. However, when given in maximum dosage to guinea pigs the course of the disease was not modified.[48]

It is evident that aureomycin must have a different mode of action in the body than it does *in vitro* since it is much more effective in clinical tests than in the test tube. Primarily it is bacteriostatic in action but in higher concentrations it does have a bactericidal effect. Although it deteriorates rapidly at room and incubator temperatures, bacteriostasis can be maintained by adding fresh drug every 24 hours. Since this deterioration is fairly constant for any organism the content of aureomycin in body fluids can be rapidly assayed.[49]

Blood and serum are antagonistic to aureomycin but if there is sufficient of the drug present the organisms will be killed.[49]

In vitro tests for development of resistant strains of organisms revealed that such resistance rarely develops and when it does is generally of a low order. To date no evidence has been reported that resistant organisms produce any substance similar to penicillinase.[49, 63, 64] The sensitivity to aureomycin is retained by organisms which have developed a strong resistance to penicillin or streptomycin.[65]

Studies of the effect of aureomycin on experimental infections in animals more or less followed the pattern developed in the *in vitro* tests. Aureomycin was effective against Group A hemolytic streptococci, murine infections with type I pneumococci[49] and *E. coli*[50] in mice. Little or no protection was given mice with infections caused by *K. pneumoniae*,[49] *S. typhosa* and others of the Salmonella group.[63, 49]

Some reported that aureomycin was superior to chloramphenicol in treating mice infected with *Br. abortus*. Further studies revealed that a combination of aureomycin and dihydrostreptomycin produced the best results.[51] Relapsing fever (*Borrelia novyi*) and Weil's disease (*Leptospira icterohemorrhagiae*) in small animals were also improved by administration of aureomycin.[52]

Aureomycin is not only rickettsiostatic but also is rickettsiocidal. The rickettsiae involved in epidemic typhus, scrub typhus, Q fever, Rocky Mountain spotted fever and rickettsialpox are all sensitive to aureomycin.[53, 54]

This antibiotic also showed activity against the viruses responsible for psittacosis and lymphogranuloma venereum.[53] No activity was observed against the viruses responsible for influenza A and B, canine distemper, rabies, Newcastle disease, Venezuelan equine encephalomyelitis, MEF-1 strain of poliomyelitis,[53] vaccinia and herpes simplex.[55] The infectivity and rate of multiplication of the mumps virus were not modified by aureomycin although it did reduce or completely inhibit the production of viral hemagglutinin.

III. Pharmacology

Aureomycin has a low toxicity and practically no side reactions. When given orally to mice it was tolerated in doses as high as 1500 mg./Kg. and to rats, 3000 mg./Kg. In mice the intravenous LD_{50} was 134 mg./Kg. and for rats, 118. Similar toxicity was shown by the alkaline form (pH 8.5). No untoward symptoms were observed in dogs, cats, rabbits, guinea pigs and mice given intravenous doses of 50 mg./Kg. (pH 8.5) at a rate of 10-20 mg./Kg./minute. No methemoglobin formation was observed. The only untoward reaction observed when multiple intravenous doses of 20 mg./Kg. were given to dogs twice daily for 6 days was irritation of the perivascular tissues at the site of injection. Although subcutaneous and intra-

muscular injections caused irritation only mild irritation was observed following instillation of 0.5 per cent solutions in 0.9 per cent saline into the conjunctival sacs of rabbits. No evidence of chronic toxicity was observed in mice, rats and dogs given 100 to 200 mg./Kg. daily orally for 12 weeks. No essential changes in blood pressure or respiration were produced when aureomycin at a pH of 8.5 was given to dogs intravenously, 10 mg./Kg./minute. Almost similar tolerance was observed with the hydrochloride at a pH of 2.5; however, hemoglobinuria was produced by doses of 30 to 40 mg./Kg. of the hydrochloride or by an equivalent quantity of hydrochloric acid. No such reaction was observed with aureomycin at pH 8.5 even with doses of 100 mg./Kg. Experiments with cats revealed similar tolerances to those with dogs.

Aureomycin has no modifying action upon the vasomotor action of epinephrine, acetylcholine, histamine or upon the effect of vagal stimulation of the heart. No appreciable changes were observed in the electrocardiograms of dogs given doses of 5 to 50 mg./Kg. (pH 8.5) intravenously at 5 to 10 mg./Kg./minute. Aureomycin is about one third as active as caffeine as a diuretic. It does not produce albuminuria. The blood sugar, isolated intestine or uterus are not affected. Histamine is not potentiated or inhibited. No antipyretic effects are observed in rabbits or rats. It appears in the urine one hour after an oral dose and excretion continues for 6 to 12 hours. Six hours after an intravenous dose the cerebrospinal fluid exhibits effective therapeutic concentrations.[55]

The most recent effect reported for aureomycin is that it accelerates growth of animals by as much as 50 per cent. Further work is being done on this new development.[55a]

IV. Human Studies

Doses of 0.1 to 1.0 Gm. of aureomycin were given orally and intramuscularly to adults (equivalent quantities to children) and the concentration in the blood, cerebrospinal fluid, urine and milk were measured. One hour after the intramuscular injection of 0.1 Gm. the blood levels were at a low peak with an average of 0.4 μg. per ml. and rapidly declining in the first six hours. Average maximal concentrations of 1.08 μg. per ml. were obtained about 6 hours after oral doses of 0.7 or 1.0 Gm. of the antibiotic. Urinalysis revealed concentrations as high as 128 μg. per ml. in 2 to 4 hours after oral administration. Tests of the cerebrospinal fluid of 6 of the 9 patients revealed low levels of 0.05 to 0.13 μg. per ml. corresponding to levels of 0.13 to 4.0 μg. per ml. in the blood. With a blood level as high as 2.0 μg. per ml. no aureomycin was found in the milk of one patient tested.[56, 57]

Further studies by other workers revealed that following oral administration of doses up to 1.0 Gm. given every 6 hours the plasma level usually reached 2.0 μg. per ml. Urinary excretion of the antibiotic was at a maximum in 4 to 8 hours after administration. They found concentrations as high as 256 μg. per ml. Excretion continued for 2 or 3 days after only one oral dose of 0.5 or 0.75 Gm. Using rather crude methods it was possible to recover antibiotic activity equal to 12 or 15 per cent of the single dose. *In vitro* tests revealed that bile did not inhibit aureomycin but in the body none could be recovered from the bile.[58, 59]

Still other investigators found a maximum concentration of 0.3 to 2.5 μg. per ml. in the serum within 2 to 4 hours following an oral dose of 1.0 Gm. When aureomycin was given regularly every 4 to 6 hours for a period of time cumulative effects were observed in most cases. In a 6 hour period levels as high as 20 μg. per ml. were observed. After intravenous administration of 0.05 Gm. the concentration in the serum reached 0.6 to 5.0 μg. per ml. within 5 minutes, declining gradually in the following 6 hours. Serum concentrations could not be measured after 0.05 to 0.2 Gm. of aureomycin was given intramuscularly in most patients. Only 1 out of 21 tests showed a level of more than 0.15 μg. per ml. following intramuscular injection. Tests of the cerebrospinal fluid of 2 adults given a dose of 1.0 Gm. and a child given 2.0 Gm. in 24 hours revealed

no measurable quantities of the drug.[60]

Innumerable tests by other investigators confirmed these findings.[61-69] Thus it is certain that aureomycin in the active state is excreted in large quantities in the urine. Very little enters the cerebrospinal fluid. Because of the inaccuracy and non-uniformity of the present methods for determining aureomycin the fate of the drug can only be roughly determined.

V. Administration and Dosage

From the experimental studies plus the factor of convenience it is obvious that oral administration is more advantageous than the parenteral routes. The intravenous route is also recommended but until the introduction of a new vehicle for its administration it was quite painful and was followed in many cases by thrombophlebitis. Because the hydrochloride of aureomycin required almost 5 ml. of water to dissolve 50 mg. intramuscular injection of such an acid solution also was very painful.

Thus the oral route has been used primarily. The dosages given orally have varied from 30 to 100 mg./Kg. of body weight at intervals of 1 to 6 hours. However, the recommended standard dose now is 1 Gm. every 6 hours or a total of 4 Gm. daily if the patient is an adult of average size and is acutely ill. In critical cases this may be increased to 6 Gm. on the first day. In 2 or 3 days the dosage is reduced to 2 Gm. or less if the patient shows considerable improvement. In some patients nausea may accompany the administration of aureomycin. In such cases the dose and the interval of time between dosages should be decreased. Administration of milk, aluminum hydroxide gel, phenobarbital and other similar agents have been helpful in alleviating the nausea. Very rarely does the nausea necessitate discontinuance of the drug. Very recently hypersensitivity to aureomycin was reported. Of 3 patients given 250 mg. 3 or 4 times daily for 8 days to 5 weeks one developed an acute generalized urticaria, another an erythema multiforme-like eruption and the third an eczematoid eruption in the groin and scrotum. Withdrawal of the drug caused a subsidence. Desensitization with small doses was not successful.[69a]

When aureomycin was first made available intravenous injection of it was very painful. Now there has been introduced a new vehicle, L-leucine, which eliminates this disadvantage. Five ml. of the vehicle or diluent contain 131 mg. of leucine into which can be dissolved 100 mg. of aureomycin hydrochloride. It alone may be injected very slowly or it may be added to an isotonic saline or dextrose infusion. By this means 400-500 mg. may be given in 12 hours to a patient who is seriously ill.

If in certain instances intramuscular injection is the indicated method, 30-50 mg. of aureomycin should be dissolved in 3-5 ml. of liquid along with the usual dosage of procaine and given at 6 hour intervals. Procaine will diminish somewhat the pain due to the acidity. Buffer solutions should not be added to the solution since they will cause the aureomycin to lose some of its potency.[38]

VI. Indications

The indications for therapy with aureomycin are numerous. It has shown some effect in the following diseases: amebic colitis, syphilis, pneumococcal pneumonia, meningococcemia, gonococcal urethritis, localized staphylococcal infections, brucellosis, tularemia, urinary tract infections, pulmonary tuberculosis, the rickettsial diseases, diseases due to filtrable viruses, ocular infections, granuloma inguinale and herpes zoster.

A. Amebic Colitis

In a study of 14 cases of amebic colitis treated with aureomycin given orally rapid cures were reported. Examination of the stools revealed no organisms present in a few days and the symptoms disappeared rapidly. *In vitro* tests with strains of amebae isolated from 3 of the patients revealed that aureomycin is amebicidal in its activity.[65-65c]

B. Syphilis

Aureomycin has been used in treating 2 cases of acute syphilis. The results obtained

were comparable to those when penicillin is given.[64]

C. Brucellosis

Aureomycin has shown considerable promise in the therapy of brucellosis caused by any one of the three organisms, *Br. abortus, Br. suis* and *Br. melitensis.* [46, 47, 66, 67] Administration of aureomycin resulted in a normal temperature and a prompt subsidence of symptoms and signs in 2-5 days. Tests of the blood by means of cultures revealed a prompt disappearance of organisms. Various dosages were used but good results were achieved with doses as low as 1.0-2.0 Gm. per day.[67] One group of investigators observed a sudden rise in temperature in 8-12 hours after beginning therapy sometimes accompanied by symptoms of shock. As a result they recommend that the therapy be given over a period of 11 days as follows: first day—0.1 Gm. in divided doses; second day—0.6 Gm.; third day, 1.6; and for the remaining 8 days, 2.0 Gm. daily.[47] Other workers have found that 3.0 Gm. of aureomycin orally and 2.0 Gm. of dihydrostreptomycin intramuscularly daily for 11 to 15 days produced excellent results.

D. Tularemia

Aureomycin produces prompt and striking improvement in tularemia. The results are comparable to, and as satisfactory as, those when streptomycin is administered. Three patients, one critically ill, responded favorably to therapy with this drug.

E. Ocular Infections

When used as the borate in a 0.5 per cent solution and applied locally, aureomycin has produced excellent results in conjunctivitis caused by pneumococcus, staphylococcus, *H. influenzae,* and Morax-Axenfeld bacillus. Herpetic conjunctivitis, inclusion conjunctivitis, trachoma and various virus infections of the conjunctiva and cornea have been treated with favorable results. In 27 patients suffering from epidemic keratoconjunctivitis only 8 responded to aureomycin therapy. However, this response is more promising than that from any other agent.[70, 71]

Recently it was reported that 7 cases of dendritic inflammation were cured by instillation into the conjunctival sac of a 0.5 per cent solution of aureomycin. The antibiotic was given every 1-2 hours while the patients were awake. Within 1 to 2 days the symptoms began to subside. Healing of the cornea occurred in 4 to 21 days depending upon the size of the original corneal defect. Two cases of herpes zoster ophthalmicus with corneal ulcer also were treated successfully.[72]

F. Bacillary Urinary Tract Infections

Aureomycin has shown effectiveness in the therapy of 2 cases of urinary tract infection caused by *A. aerogenes* and *E. coli.*[68] Other investigators have reported successful cures in urinary tract infections due to *A. aerogenes, E. coli, Proteus* and *Ps. aeruginosa.* Some of these also were complicated by the presence of *S. viridans* and *S. fecalis.*[45] Some workers confirm these findings but report that the effect of aureomycin on infections caused by *Ps. aeruginosa* and Friedländer's bacillus outside of the urinary tract has not been impressive.[56] Recently success has been reported in treating 10 children, 8 with *E. coli* infections and 2 with mixed hemolytic *S. aureus* and *E. coli* infections. All but 1 case had been treated unsuccessfully with other drugs. Aureomycin was given in doses of 30-60 mg./Kg. daily in divided doses every 4 hours for 4-8 days. In 9 patients the urine was negative in 38-48 hours and in 1 in 4 days. Relapses occurred only in those treated for 4 days.[72a]

G. Typhoid Fever and Salmonella Infections

Aureomycin shows little value in typhoid fever and in infection by the Salmonella group of bacteria.[56, 73] One group has concluded that aureomycin is much less effective in typhoid than is chloramphenicol, which is practically a specific.

H. Rickettsial Diseases

Aureomycin has a powerful antiricket-

rsial action. Consistently successful results have been achieved by its use in treating the following: Rocky Mountain spotted fever, [61, 66, 68, 78] Brill's desease, [77] Q fever, [79] typhus,[67] and rickettsialpox.[79] It acts similarly in all these conditions. Within 24 hours after therapy is begun the patient appears more alert; the temperature is lowered; headache is relieved; and the toxemia is decreased. In 48 hours the temperature is normal and the patient improves rapidly. In some cases this may not take place for 96 hours but cure in even this prolonged time is remarkable. Aureomycin is considered far superior to para-aminobenzoic acid and equal to chloramphenicol in the therapy of the rickettsial diseases.[28]

I. Virus Infections

Thirty-five cases of lymphogranuloma venereum have been successfully treated with aureomycin and, in the opinion of these workers, this antibiotic surpassed any therapy used previously. The condition varied in the patient. Some had buboes, some acute proctitis and some rectal strictures. Within a few days after the beginning of therapy the buboes showed material shrinking and no recurrences developed later. Acute proctitis also responded and in cases where it was accompanied by recial stricture only the chronic anatomic changes remained.[80, 81] Others have reported disappointing results.[81a]

Aureomycin also has been effective in curing primary atypical or virus pneumonia. Many of the cases were confirmed by serologic tests and all followed the usual clinical course of this disease. In many cases penicillin had shown no effect. The symptoms subsided within 18 to 24 hours and in 48 hours the temperature had returned to normal. [82-85] If the drug is discontinued at this time relapse usually occurs but further therapy will control the condition again.[28] Various common respiratory tract diseases such as the common cold, nonbacterial exudative tonsillitis and pharyngitis, acute infectious croup, and primary bronchitis have been treated successfully with aureomycin.[82a] A recent report states that 28 patients with whooping cough were treated with aerosol of aureomycin with good results when used in the first 2 weeks.[85b]

J. Miscellaneous Diseases

Treatment of pneumococcal pneumonia with aureomycin results in improvement similar to that achieved with penicillin.[29, 56, 85a] One case of meningococcemia has been reported as treated with aureomycin with striking results.[64] Aureomycin was reported to be inferior to penicillin in treating 60 cases of gonococcal urethritis but this may have been due to the small doses given.[58] In another study in which the cure rate was only 70 per cent as compared to 95 per cent with 75,000 units of procaine penicillin in oil it was thought that the use of alcoholic beverages might have affected the activity of the aureomycin.[64b]

Several cases of localized staphylococcal infections treated with aureomycin have been cured. In 2 instances diagnosis was confirmed by positive blood cultures.[63, 87]

Improvement has occurred in patients having granuloma inguinale when they were given aureomycin. [81, 88]

In a recent report of treatment of 16 patients it was stated that totals of 10.8-70.0 Gm. given in variable schedules resulted in cures on an average of 11 days after therapy was completed. Four patients who had not responded to 1500 mg. given intramuscularly did respond to oral administration. Nausea, vomiting, diarrhea and dizziness occurred in some patients. These effects were more noticeable when the total dose of 20 Gm. was given in 5 days rather than in 10.[85a]

Aureomycin has shown some value in preoperative preparation because of its effect upon the bacterial flora of the intestinal tract.[88b]

Some report that aureomycin has little or no effect in infectious hepatitis and infectious mononucleosis.[28] In a recent report on the latter condition it was stated that hospitalization was reduced for 18 patients when given aureomycin in doses of 0.5 Gm. 4 times a day for 6 days. The average hospitalization was 44 days whereas with the aureomycin-treated patients it

was 32. The disease was terminated in less than 30 days in 72 per cent of the treated group as contrasted with 36 per cent in the control group given symptomatic therapy. Within 24 hours the fever returned to normal in 40 per cent and in 72 hours in 70 per cent. In the control group the shortest febrile period of a patient was four days, and only 56 per cent of the control patients were afebrile within 14 days of the onset of the disease. No decrease in the duration of the abnormal leukocyte and differential blood cell counts was observed but enlargement of the spleen did not occur in 80 per cent of the patients who were given aureomycin during the first 10 days. Although this is only a preliminary study it appears to indicate that aureomycin has some value in infectious mononucleosis.[89]

In another report it was stated that the duration of the disease was just as long in those given aureomycin as in those given placebos. In addition, a large number experienced unpleasant side effects.[89a]

Recently it was reported that 80 to 90 per cent of rats and dogs subjected to x-radiation died of hemorrhages and infections whereas in a group exposed to x-radiation and treated with aureomycin 80 per cent survived. Thus it is possible that aureomycin may have some effect in combatting radiation sickness.[90]

Aureomycin has been reported to be more than twice as effective as penicillin, weight for weight, in treating experimental leptospirosis.[91] Recently a clinical case was reported in which massive doses of penicillin were given for 36 hours and the patient sank into a comatose and apparently moribund state. Along with symptomatic therapy the patient was given an initial dose of 2.0 Gm. by Levin tube followed by doses of 250 mg. every 3 hours. Twelve hours later the dosage was increased to 500 mg. every 3 hours and continued until a total of 17.25 Gm. had been given. Within 12 hours after aureomycin therapy was begun the patient showed improvement and finally recovered. Because the penicillin was continued for a time after aureomycin therapy was begun the recovery was not entirely attributed to aureomycin but it certainly had a striking effect because the patient was growing rapidly worse with penicillin alone.[92] A similar case has been reported.[93]

A recent report has revealed that aureomycin was effective in curing 2 cases of meningitis resulting from complications in the surgical exposure of the spinal cord. The organisms involved were *Bacillus pyocyaneus* and *aerogenes*. In one case aureomycin was given intravenously twice daily in doses of 0.1 Gm. in diluted sodium lactate for a week and also rectally in doses of 3 Gm. daily. The cerebrospinal fluid became sterile during the week. In the second case it was administered in doses of 1 mg. in 1 cc. of sodium lactate solution intraventricularly followed by 10 mg. in 10 cc. of solution a few hours later and repeated for 9 days. During 3 of these days it was given intraspinally. On the third day the spinal fluid was sterile and on the eighth the ventricular fluid was sterile.[93a]

Aureomycin has been tested for its effectiveness against such conditions as rheumatoid arthritis, Hodgkin's disease, periarteritis nodosa, lupus erythematosus disseminatus, ulcerative colitis and Guillain-Barré syndrome but no benefits have been observed. Some have used it in herpes zoster and herpes simplex with good results. Others report it to be of little or no value in the former and of no effect in the latter.[89]

There have been further reports recently of the use of aureomycin in treating certain mouth diseases. In 289 patients receiving a total of 902 dental treatments, some involving the use of a rubber dam, only 4 lesions of herpes labialis developed in less than 2 days when a 5 per cent aureomycin hydrochloride ointment was applied before and after treatment. In some patients it was also used after meals and after washing the face for 3 days. In a series of 311 patients with 1,264 procedures treated with a plain petrolatum ointment 28 lesions developed. If the lesions had already developed aureomycin hydrochloride ointment shortened the duration by 4 days in many cases. Thirty-eight patients with recurrent oral aphthae were given 1 troche of 15 mg. of the hydrochloride every 2 hours while

awake for 3 days and the duration of the lesions was shortened by 3.7 days. The reduction was more marked when therapy was started in less than 24 hours after the eruption developed.[90c]

In another series oral aureomycin in troche or capsule form gave marked relief in less than 24 hours in 45 patients with necrotic gingivitis which was acute in 2 and chronic in 3, associated with Vincent's angina in 5, with pharyngitis in 14, with arthritis in 1, and in 2 with soft palate inflammation of unknown origin. Gingival bleeding was stopped in 48 hours and healing occurred in 4-8 days. The drug was given every 2-4 hours until healing occurred. In pharyngitis the throat condition was improved in 6 hours and completely relieved in 24-36 hours by aureomycin. When aureomycin hydrochloride in 25 mg. cones was applied subgingivally to the periodontal pocket in patients with chronic suppurative pericementitis the inflammatory symptoms and suppuration were greatly reduced. Similar results were obtained with troches as well. Pain was alleviated and inflammation reduced in patients with pericoronitis and periodontal abscess in whom the cones were applied. Healing was promoted in 16 patients in whom the cones were applied in the sockets after extraction of acutely abscessed or infected teeth but the cones were not absorbed and in some cases a foreign body reaction occurred. Improvement was reported in several other related mouth diseases. In some cases there were toxic reactions which were eliminated by replacing the 250 mg. capsules with troches.[90d]

Three cases of chancroid have been healed by giving 0.5 Gm. of aureomycin 4 times a day for 4-14 days. However, it is not recommended except in specific instances because of its masking effect on syphilis.[93b]

No improvement was observed in 3 cases of pulmonary tuberculosis to whom aureomycin was given. However, when it was discontinued and streptomycin therapy was begun the usual response was observed.[94, 95]

The use of aureomycin in otitis media also has been reported. In 2 patients with early catarrhal otitis media the symptoms completely subsided in 24 hours. One patient with purulent otitis media did not respond. Penicillin, sulfadiazine and aureomycin were necessary for improvement in 1 week in a child with bilateral otitis media.[93a]

In a study of various skin conditions it was found that aureomycin should be given in treating pemphigus only when penicillin is unsuccessful.[93b]

Three cases of peritonitis caused by ruptured appendix and one caused by perforated ulcer were treated postoperatively with aureomycin and one case of perforated intestine during typhoid fever without operation was treated with aureomycin. An initial oral dose of 3 Gm. of aureomycin was given 1 to 3 days after signs of peritonitis were evident. Further treatment consisted of 0.25 Gm. every 2 hours for 2 days and then 0.25 Gm. every 4 hours for 3 to 5 days. All of the cases recovered. The typhoid fever, however, was not affected although the peritonitis was cleared as a result of the aureomycin therapy.[90c]

In a series of infants with diarrhea aureomycin was believed to give better results than chloramphenicol.[27a]

Terramycin

One of the newest antibiotics to be made available is terramycin, a product derived from the mold, *Streptomyces rimosus*.[96] It too, like chloramphenicol and aureomycin, has a wide antibacterial spectrum.

I. Properties

Terramycin is amphoteric and is capable of forming the crystalline hydrochloride and sodium salts. It melts with decomposition at approximately 185° C. It is soluble in methanol, ethanol, acetone and propylene glycol. In water 0.25 mg. may be dissolved per ml. at 25° C. It is insoluble in ether and petroleum ether. One outstanding advantage in its properties is that it is stable over long periods of time in aqueous solutions at an approximate pH of 2.0 to 5.0, at room temperature. In the dry crystalline state this antibiotic and its

salts are highly stable at 25° C. At 50° C. it may be stored for as long as 8 weeks and at room temperature for 12 months without significant loss of potency. A terramycin unit is defined as one microgram of the pure anhydrous amphoteric compound. The activity is expressed in terms of the equivalent weight (μg.) of crystalline terramycin needed to inhibit growth. The activities of the salts of terramycin are stated in terms of the equivalent weight of pure amphoteric terramycin.

II. Experimental Studies

Terramycin, like aureomycin and chloramphenicol, is active both *in vitro* and *in vivo*. *In vitro* tests have revealed that terramycin has 100 per cent inhibitory activity in the concentrations indicated against the following organisms (concentration expressed in μg./ml.): *Aerobacter aerogenes*, 1.0; *Klebsiella pneumoniae*, 3.0; *Escherichia coli*, 5.0; *Salmonella typhosa*, 3.0; *S. paratyphi*, 1.0; *S. schottmuelleri*, 1.0; *S. pullorum*, 10.0; *Shigella paradysenteriae*, 1.0; *Bacillus subtilis* (FDA 219), 3.0; *Staphylococcus albus*, 1.0; *S. aureus*, 1.0; *Proteus sp.* 1000; *Pseudomonas aeruginosa*, 100; and *Brucella bronchisepticae*, 3.0.[96]

In vitro studies show that the following are organisms susceptible: most strains of hemolytic and non-hemolytic streptococci; many strains of enterococci such as *Streptococcus fecalis* which are resistant to other antibiotics; 30 strains of penicillin-resistant staphylococci; certain bacillary organisms; *H. influenzae* and *H. pertussis*; and *Brucella abortus, suis* and *melitensis*.

Experimental studies *in vitro* have shown that terramycin also may be of value in treating amebiasis.

Both the *in vitro* studies and animal experiments have revealed that *H. influenzae* and *H. pertussis* are highly sensitive to terramycin. In mice this antibiotic was found to have a marked suppressive effect on the course of experimental brucellosis. Terramycin is believed to be as effective as streptomycin in tularemia as evidenced by studies on mice. Laboratory tests for its effect on the various rickettsial infections have revealed that terramycin is highly effective against *R. tsutsugamushi* (scrub typhus) and *R. prowazeki* (epidemic typhus). In the chick embryo it is capable of inhibiting the rickettsia of Rocky Mountain spotted fever, which fact suggests that it may have some value in Q fever. *R. akari*, the etiologic agent for rickettsialpox, is also affected by terramycin. Terramycin, in high concentrations, has shown an inhibiting effect on the infection of the chick embryo with the PRS strain of influenza A virus.[97]

III. Pharmacology

Terramycin is a relatively non-toxic antibiotic as shown by extensive animal studies[98] and clinical observations in more than 350 patients. No toxic reactions have been observed when sodium terramycin or terramycin hydrochloride was orally administered to dogs in dosages of 80 to 500 mg./Kg. of body weight. Some toxic symptoms were observed, however, in a small percentage of animals given 80 to 160 mg./Kg. of body weight of sodium terramycin intramuscularly over long periods of time.

Studies of the absorption and excretion of terramycin in dogs and rabbits have indicated that it is absorbed rapidly throughout the body when given orally or parenterally. It is excreted in a biologically active form.[99]

IV. Human Studies

In the first studies of terramycin in man 5 fasting subjects were given single oral doses of 25 to 50 mg./Kg. of body weight which produced peak serum concentrations in 2 to 4 hours. The average maximum concentrations determined were 18.0 mg. per ml. after a dosage of 25 mg. and 40 mg. per ml. after a dosage of 50 mg./Kg. of body weight. On an average 47 per cent of the total dose was excreted in a biologically active form.

Further studies on 23 adult patients indicated (a) that maximum concentrations of terramycin may be detected in the serum of most patients receiving single

oral doses of 25 to 50 mg. of terramycin hydrochloride per Kg. of body weight, within 2 hours after administration; (b) that the maximum concentrations achieved after administration of such doses are 5 to 6 and 10 to 20 μg. per ml. respectively; (c) that after maximum serum concentrations are attained, the levels remain at a plateau for 2 to 4 hours and then decline; (d) that the drug is present in high concentrations in the urine within 2 hours after administration.

In 13 patients given maintenance doses of 4 to 5 grams daily in divided dosage once every 6 hours the serum concentrations varied from 2.5 to 12.6 μg. per ml. Two to 25 per cent of a single oral dose was excreted in the first 24 hours.[100, 101]

As a result of the pharmacologic studies on animals and the various clinical observations it is recommended that terramycin be given by the oral route only at present. The maximum daily dosage recommended is 100 mg./Kg. of body weight and the average daily dose, 33 to 50 mg./Kg. of body weight.

In clinical trials the maximum single dose administered has been 3.25 Gm. or 49 mg./Kg. of body weight. The maximum total dose given was 125 Gm. or 1.25 Gm. every 6 hours for 25 days. No untoward effects were reported. Another group of subjects have been given 5 Gm. of the hydrochloride daily for about 1 month with no untoward effects.

Mild gastrointestinal disturbances have been observed in a small percentage of patients. Looseness of the stools was the most common reaction reported. In some cases there was mild nausea and vomiting which in most instances occurred when the drug was taken on an empty stomach. By administering terramycin just prior to a light meal these reactions usually were avoided. When nausea and vomiting did occur they usually were more severe in the first day or two and then disappeared. It has been suggested that the frequency and severity of these reactions may vary directly with the size of the daily dose since no such reactions occurred following dosages of 1 to 2 Gm. daily.

A few patients reported glossitis with or without lesions. Thus far no allergic reactions have been reported but they are a possibility. In such instances mild reactions should not contraindicate continued use of terramycin. If they are severe and cannot be controlled by the usual therapy administration of terramycin should be stopped.

V. Indications

Terramycin is indicated in the therapy of diseases caused by many of the Gram-positive and Gram-negative bacteria, both aerobic and anaerobic; the rickettsiae and certain viruses.[97] At present, the recommended oral dose is 2 to 3 Gm. daily in divided doses given every 6 hours for acute infections. For severe infections double the quantity may be necessary. Adult and children's dosages are the same. Just as with the other antibiotics the dosage in many cases will need to be adjusted for the patient. Therapy should be continued for at least 48 hours after the temperature has returned to the normal level and the acute symptoms have disappeared. All dosages mentioned are in terms of weight of pure terramycin.

a. Bacterial Infections

Terramycin has been shown clinically to be highly effective in treating acute lobar pneumonia. Satisfactory response was observed in practically all of more than 75 patients treated. The dosage given varied from 1—5 Gm. daily. Within 24 to 48 hours the temperature had returned to normal. To avoid the possibility of relapses therapy was continued for 3—10 days. This varied with the nature and severity of the infection. The recommended dosage is therefore 2—3 Gm. daily in divided dosage every 6 hours.

One patient with pneumococcal peritonitis became afebrile within 36 hours after administration of 3 Gm. daily. Therapy was continued for 9 days.

A daily dosage of 4 Gm. in divided doses every 6 hours produced satisfactory results in 10 cases of primary pneumonia due to mixed bacterial floras (*Staphylo-*

coccus aureus, Streptococcus hemolyticus, Streptococcus viridans, pneumococcus, and others.

Five cases of acute follicular tonsillitis and 3 cases of acute hemolytic streptococcal sore throat have been treated successfully with dosages of 2 to 4 Gm. daily in divided dosages every 3—6 hours. One case of erysipelas given 5 Gm. daily (divided) for 9 days responded favorably. One patient with a perirectal abscess caused by anaerobic streptococci and one with cellulitis were treated successfully with 2 Gm. daily. One patient with a urinary tract infection caused by *S. hemolyticus* responded to a dosage of 3 Gm. Four to 6 Gm. daily brought about symptomatic improvement and a fall in temperature in a patient having subacute bacterial endocarditis, caused by a micro-aerophilic streptococcus.

One patient with chronic pyelonephritis and one with an urinary tract infection due to enterococci showed symptomatic and bacteriologic response when given 2 and 4 Gm. daily, respectively. It remains to be seen whether this will continue when the drug is stopped. One case of pyelonephritis caused by enterococci and *Ps. pyocyaneus* also responded to therapy with 4 Gm. of terramycin daily for 2½ days and 2 Gm. daily for another 3½ days.

Certain staphylococcal infections also respond to therapy with Terramycin. One case of staphylococcal conjunctivitis and 2 cases of urinary tract infections caused by staphylococci in which the organisms had developed resistance to penicillin responded satisfactorily to terramycin therapy. One patient with a breast abscess caused by *M. pyogenes* responded immediately to a dosage of 4 Gm. daily (in divided dosage) for 3½ days. Sterilization of the blood stream occurred after therapy with 6 Gm. of terramycin daily in one patient having staphylococcal sepsis, brain abscess and questionable endocarditis. Terramycin therapy produced no response in another patient suffering from staphylococcal subacute bacterial endocarditis.

In acute gonorrhea terramycin therapy has been shown to be highly effective. In a group of 48 patients treated with single oral doses of 250 mg. to 2 Gm. response was prompt. In another series of 22 patients 18 responded promptly within 24 hours to a single dose of 1 Gm. One responded after further therapy with 0.5 Gm. doses every 6 hours for 3 doses. The 3 remaining patients were not given terramycin again. A 1 Gm. dose of terramycin should be sufficient to cure most cases of acute gonorrhea. In those instances where response is not prompt further therapy with 0.5 Gm. every 6 hours for 3 to 4 doses is recommended. Thus far no clinical data are available concerning the necessary dosages for chronic gonorrhea or for cases with complications such as arthritis, prostatitis, epididymitis, and salpingitis.

In a recent report terramycin was shown to effect a satisfactory cure rate in the treatment of gonorrhea despite the fact that the dosage required was somewhat higher than that for chloramphenicol. From 1 to 2 Gm. of terramycin hydrochloride in divided doses gives a cure rate of 80 to 100 per cent, while single doses of 750 mg. of chloramphencol give similar cure rates.[102]

Prior to treatment for gonorrhea, dark-field examinations of the exudate from any primary lesions should be made in the event that syphilis may be the cause since therapy with terramycin masks the early signs of syphilis. In suspected cases serological tests should be done monthly for at least 3 months.

Terramycin, clinically, has shown excellent results in the therapy of acute brucellosis. In a series of 11 patients with acute brucellosis prompt response has been observed with dosages of 50 (1 case), 100 (7 cases), and 150 (2 cases) mg. per Kg. body weight per day for a period of 5 to 10 days, followed by 50 mg. per Kg. body weight per day, in all instances, for a total of 28 days of therapy. One patient received only 2 grams daily from the start of therapy. The temperature dropped to normal levels in all cases and improvement in the disease occurred within 1 to 3 days. All symptoms subsided very soon after the

first 3 days. Thus far no information is available as to possible incidence of relapse.

In infections caused by terramycin-sensitive gram-negative organisms such as *K. pneumoniae* (Friedländer's bc.) and urinary tract infections due to *E. coli, A. aerogenes,* and others, this antibiotic has been shown to be highly effective. Thus far the effective dosages have varied from 1—5 Gm. daily. It is believed that 2 to 3 grams daily in divided dosage should be sufficient for the treatment of most urinary tract infections due to terramycin-sensitive organisms. If response is not prompt, higher dosages should be used. In dosages of 2 to 5 Gm. daily ferramycin has given satisfactory results in two cases of pneumonia due to *K. pneumoniae,* one patient with pyelonephritis (*A. aerogenes*), and one case each of endometritis (*A. aerogenes*), pyelonephritis (*E. coli*), and acute cystitis (*E. coli*). Penicillin therapy was ineffective in one patient with a diffuse bronchopneumonia due to *E. coli* and *Neisseria,* but when the patient was given terramycin in doses of 4 Gm. daily for 8 days he was freed of the infection. Still another patient suffering from multiple liver abscesses and septicemia due to *A. aerogenes* showed prompt sterilization of the blood stream after terramycin was given in daily doses of 5 Gm. However, an elevated temperature persisted even after 35 days of therapy.

No clinical data are as yet available as to the effectiveness in the therapy of tularemia in humans. This also applies to the therapy of syphilis although the available studies indicate that a single dose of 60 mg. per Kg. body weight is sufficient to reverse the dark-field in a high percentage of individuals.

b. Rickettsial Infections

Four Gm. of terramycin for one day were sufficient to bring about a satisfactory response in a patient with scrub typhus. In 3 patients with murine and 1 with epidemic typhus response was observed to daily dosages of 100 to 200 mg. of terramycin per Kg. body weight for 5 to 8 days. The optimum dosage has not yet been determined.

Terramycin, in laboratory studies, has been shown to have considerable action against Rocky Mountain spotted fever and Q fever but no clinical reports are as yet available. In 4 cases of rickettsialpox 5 Gm. daily doses (divided) for 3 days has produced a satisfactory response in 24 to 48 hours.

c. Virus Infections

Eight cases of primary atypical pneumonia have been treated successfully with doses of 1—5 Gm. daily. However, it is believed that 2 grams daily in divided dosage should be adequate for the treatment of this infection. The response has been prompt and in most cases the temperature has returned to normal within 24 hours.

From a preliminary test of 4 to 6 patients with herpes zoster it is possible that terramycin may be effective in doses of 2—6 Gm. daily for 6 days. One case of lymphogranuloma venereum was cured by a dosage of 1 Gm. administered once every 6 hours (4 grams daily) for a period of 13 days.

Satisfactory results have been achieved in 5 cases of granuloma inguinale given 1.5 to 4 Gm. daily in divided dosage for 12 to 15 days.

Because *in vitro* studies indicate possible value, terramycin is being tested for its clinical value in controlling influenza.

d. Miscellaneous Infections

Satisfactory response has been observed in one patient with anthrax within 24 hours after start of therapy, on a dosage of 100 mg. per Kg. body weight per day.

Thus far only one patient with an acute laryngotracheal bronchitis, from whom *H. influenzae* was isolated, and 5 patients (including 1 infant) with whooping cough (pertussis) have been treated with terramycin. Administration of 5 Gm. daily for 3½ days brought about improvement in the first case and in the latter 5 patients reversion of cultures and symptomatic improvement within 24 to 72 hours after start of therapy was observed. Until further clinical evidence is available oral

terramycin therapy is not recommended in the treatment of *H. influenzae* meningitis or other serious infections due to this organism.

To date terramycin has produced successful results in the therapy of one case of *erythema multiforme bullosa* (4 Gm. daily for 13 days), one case of catarrhal conjunctivitis with fever (4 Gm. daily for 6 days), one case of Reiter's syndrome, and two cases of bacteroides bacteremia. *In vitro* studies indicate its possible effectiveness in treating amebiasis.

In a recent report terramycin was given to 30 patients suffering from one of the following: pneumococcic pneumonias, urinary tract infections due to *Escherichia coli* and *Aerobacter aerogenes*, whooping cough, bacteremia due to *Salmonella choleraesuis* var. Kunzendorf, pneumonitis and lung abscess with mixed bacterial infections. Within 1 hour assayable quantities were found in the blood and urine and for five hours after the administration of 750 mg. of the drug by mouth.[102]

Terramycin is of questionable value in Salmonellosis and particularly typhoid fever as shown by the fact that of 13 cases of Salmonellosis of which 6 had typhoid fever no response was shown to 100 to 200 mg. Kg. of body weight of drug. Better results were obtained in 3 patients with infections due to *Salmonella choleraesuis* var. Kunzendorf.

In vitro and *in vivo* studies have shown that most strains of *Ps. pyocyaneus* are highly resistant to the action of terramycin. However, there are occasional instances in which certain strains of *Ps. pyocyaneus* may be encountered which are sufficiently sensitive to terramycin to respond to therapy. There is no evidence to date that such strains of *Proteus vulgaris* may exist.

Terramycin is definitely of no value in the therapy of measles, mumps, malaria, trichinosis, and variola. Despite the *in vivo* studies in animals showing tuberculostatic activity this to date is not proven and therefore terramycin is not indicated. Likewise it is not indicated in meningitis and in endocarditis due to penicillin-sensitive organisms.

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104. Terramycin is available in capsules of 50, 100 and 250 mg. from Chas. Pfizer and Co., Inc.

Cortisone Now Available For Wide Hospital Usage

Cortisone, found to be beneficial in the treatment of rheumatic diseases, has been made available for its first widespread distribution to U. S. hospitals.

Merck & Co., first to produce the drug by chemical synthesis, said it had obtained approval from the Food and Drug Administration to allot its increased supplies now to some 6,500 hospitals registered by the American Medical Association.

The drug is being manufactured under the trade name of Cortone, the company said.

Learn the Indirect Method for Endolaryngeal Operations

(A reminder).

Emil Glas, M.D.*
New York, N. Y.

I am an oldtimer and came from Vienna which is known as the cradle of laryngoscopy. Some years ago I wrote a historical paper on the development of laryngoscopy and a historical paper on the development of laryngoscopy and endolaryngeal work and mentioned the steps and impasses encountered years ago until a good result was achieved. *Liston*[1] (London) and the Spaniard *Manuel Garcia*[2], a singing teacher in London, had looked into the larynx and had done important preliminary work, but *Tuerck*[3, 4] and *Czermak*[5] were the first to study the matter in a very broad way and are called the discoverers of laryngoscopy. *Garcia* wrote the following in his little publication on this subject: "The method which I have adopted is very simple; it consists in placing a little mirror, fixed on a long handle, suitably bent, in the throat of the person experimented on against the soft palate and uvula. The party ought to turn himself towards the sun so that the luminous rays, falling on the little mirror, may be reflected on the larynx. If the observer experiments on himself he ought by means of a second mirror to receive the rays of the sun and direct them on the mirror which is placed against the uvula." *Czermak*[5] made himself independent of sunlight and introduced artificial light, a modification certainly of great importance. Although in the first years great difficulties were encountered and no means were available of anesthetizing the mucous membrane of the larynx, some operative trials to remove polyps of the vocal cords were made. *Czermak* was the first to emphasize that the eye of the laryngologist had to be the guide of the operating hand, and he did some endolaryngeal operative work with good results. The development of the endolaryngeal operative art took a long time but the pioneers finally reached their goal and when *Charles Koller*[6], the Viennese ophthalmologist (who later on came to New York), and *Jelinek*[7], a laryngologist, introduced cocaine as an anesthetic agent into the technic of eye and laryngeal work most of the impasses and difficulties were removed. Anyone, who after the cocainisation of the larynx is able to remove a polyp or a fibroma from a vocal cord, certainly enjoys his work. *Garcia*[8] once mentioned that "however dexterous we may be in exposing the vocal cords and even when we are most successful, unfortunately at least a third of the anterior part of the glottis remains concealed by the epiglottis." *Czermak* confirmed this difficulty by mentioning that the epiglottis covers a great part of the anterior area of the vocal cords, but he hoped that some improvement in the technic could overcome this impasse. The modern laryngologist with no difficulty reaches the anterior commissura by pressing the handle of the instrument against the laryngeal part of the epiglottis and lifting the cartilage against the base of the tongue. I shall never forget the astonished question of a citizen of Galicia,

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who, after having been operated in some seconds and then hearing of the fee he was to pay, said: "Going in and out in some seconds and then so much to pay!"

Years after came direct laryngoscopy (endoscopy) and as is generally known the German laryngologist *Gustav Killian*[8] was the inventor of the bronchoscope. We, the older laryngologists[9], began using bronchoscopy for diagnostic purposes and for removal of foreign bodies from the deeper passages of the respiratory tract, but we still adhered to the good old indirect method for removing small growths from the vocal cord, the anterior commissure, the interarytenoid space and from the subglottic area. But the modern school no longer bothers with the indirect method for endolaryngeal operative work, and now I very often see a large armamentarium for the removal of a small wart on the vocal cord. If we compare the two methods, the indirect is absolutely to be preferred and the laryngologist of today should certainly learn this method in addition. In the beginning it may be a little difficult because of the localization and the reversed picture, but when properly learned it will certainly satisfy the ambitious student. I remember many years ago the embarrassment of a young but capable doctor I taught, who, surrounded by other colleagues, tried to remove a polyp of the right ventriculus Morgagni and stayed in the larynx with his forceps quite a long while, trying to grasp the polyp again and again (having a fight with the epiglottis which covered the area) and finally giving up. He said he did so to avoid doing damage to the mucous membrane of the larynx. And he was right. The technic must be learned and learned again on the specimen, on the cadaver and on the cocainized patient. After this training a careful and skillful worker will certainly find no difficulty in doing this work. Once in a while a growth which is subglottically located or hidden near the anterior commissure may occasion some impasse which certainly would be overcome by a well trained laryngologist.

If it is asked why we prefer this indirect method to the direct the answer is because the operation can be done in the office, without excitement and without any great preparation. The agitation and nervousness due to hospital surroundings are also avoided. The normal position of the patient for the direct laryngoscopy is the horizontal with the head bent over the edge of the table, a position very uncomfortable to the patient. When I see it done this way I always have the feeling that too big guns are being used for very small targets. Besides, it is not to be forgotten that some damage could be done—and I have seen it done—by such manipulations and the injury certainly can be much greater than that done by indirect laryngeal work. A small tear of the mucous membrane may have bad consequences and result in submucous inflammation, abscess formation, mediastinitis, etc. The large production of mucus can sometimes disagreeably interfere with the work and make it impossible to remove the whole growth. But the principal argument for the indirect method is the simplicity of the work when we know how to do it. And in my opinion it is our duty to choose the simple one if it can be done. I remember the question of a patient years ago from whom I removed a papilloma of the larynx in the office of another laryngologist. The first question he asked, after I took the forceps out of his mouth, was: "Why did they not use this comfortable way the first time they operated on me?"

I want to add one word about the instruments used in indirect operations. I don't like the newer, more massive instruments that have been constructed for this purpose. I prefer the old, very simple and very fine forceps of *Professor Stoerk*[10], one of the old Viennese pioneers of laryngoscopy. This instrument is easily handled and does not interfere in any way with the view of the whole operative field.

• • • •

Oldtimers with greater experience are sometimes allowed to give advice. Take

—Concluded on page 329

The Emotional Factor in Disease

J. Arthur Buchanan, M.D.
Brooklyn, N. Y.

One-third of all patients who consulted me during my years of practice were classified as suffering from emotional disturbance. In some instance the emotional disturbance was brought on by knowledge of an organic disease.

There have been many words used to indicate this problem. The most commonly used classification when I was a Fellow on the Mayo Foundation was chronic nervous exhaustion. Neurasthenia was popular for a time. The word "neurotic" was in vogue for some years. In dealing with patients, the use of these terms and similar ones, as a diagnosis for the patients' complaints, frequently led to discussions about the true meaning of the terms. Patients asked questions for which no satisfactory answers could be given. The word "neurotic" or "neurosis" was resented by many, as well as other terms that indicated physical or mental inferiority. Lately, the term "psychosomatic disturbance" has come into use, but its fundamental meaning is beyond the grasp of many patients.

In a search to find a diagnostic classification that would avoid any unpleasant reactions and that was physiological, I began using the term "emotionalism" several years ago. The questions were then posed on a sound basis, and there were no unpleasant reactions to the diagnosis. The problem was one of educating the patient to understand sensations and reactions that were normal in a particular body organization.

The types of patients presenting emotional problems have interested me deeply since my medical college days. The first patient I met in the dispensary fell in that category. The literature on the subject has always been of great interest. The subject is, of course, as old as man.

Material of This Study

This study is based on 100 patients examined and observed in my office. Seventy-seven of the patients were females. All had careful histories taken. The time devoted to obtaining histories sometimes ran into many hours. Additional data were collected while the patient was under observation. Some histories extended over years and were complete. The physical examinations were thorough and, in most instances, were repeatedly reviewed. Each patient had a blood Wassermann test, complete blood count with hemoglobin estimation, and urinalysis. In some cases a variety of other examinations were carried out to exclude, if possible, an organic disease as the sole cause of the patient's complaint. The interpretation of a complaint as an expression of emotionalism is difficult, requiring accurate analyses unless the physician wishes to be embarrassed frequently.

Age Periods

The period of life in which emotionalism is over-exercised has diagnostic as well as causal significance. The data denoting the frequency at age periods are given in Table I.

TABLE I
AGE PERIODS

Decade	No. of Patients
0-10	1
10-20	4
20-30	25
30-40	30
40-50	20
50-60	12
60-70	5

Stress has been laid on occupation as a cause of emotionalism. Many patients are advised to change the vocation as a method of curing the trouble. Table II gives the occupations of the 100 cases comprising this study.

TABLE II

Occupation	No. of Patients
Housewife	43
Clerk	10
Stenographer	9
Salesman	6
Seamstress	5
School	5
Engineer	4
Bookkeeper	3
Nurse	2
College student	1
School teacher	1
Electrician	1
Printer	1
Executive	1
Actor	1
Carpenter	1
Bartender	1
Dentist	1
None (born rich—never worked)	2

Previous Diseases

The influence of previous diseases in the production of an emotional state has some interest. In some cases, the emotional instability has its origin in the debilitated state that follows an illness, or in the anxiety factors associated with absence from the usual occupation. In some instances marked emotionalism is produced by patients being told that an organic disease exists. The types of previous diseases suffered by these 100 patients are given in Table III.

TABLE III

PREVIOUS DISEASES

Diseases	No. Female Patients	No. Male Patients
Pneumonia	10	3
Tonsillitis	32	5
Measles	54	12
Varicella	22	2
Diphtheria	17	3
Typhoid fever	2	0
Influenza	26	7
Pertussis	23	2
Mumps	21	0
LaGrippe	3	2
Acute rheumatic fever	2	2
Pulmonary tuberculosis (arrested)	1	0
Colds	16	5
Cystitis	1	0
Syphilis	1	1
Scarlet fever	7	2
Hay fever	1	2
Gonorrhea	0	2
Total No. of Illnesses	229 (2.9%)	50 (2.1%)

Physical Findings

The relative infrequency of finding definite physical abnormalities in patients suffering from emotionalism has led to many of them being told: "There is nothing wrong." In some instances minor physical changes that could be operated on are interpreted as the basis of the illness. The significant findings beyond normal in this series are grouped in Table IV.

TABLE IV

PHYSICAL FINDINGS

Abnormal Findings	No. of Patients
Overweight	4
Underweight	6
Hemorrhoids	2
Sensitive abdomen	2
Secondary anemia	2
High blood pressure	3
Low blood pressure	3
Tachycardia	1
Systolic apical heart murmur	4
Acne on face	1
Hirsutism	1
Many keratotic patches on abdomen	1
Flat feet	1
Extrasystoles	1

Surgery in Emotional Patients

The search for a cure of the sensations that disturb emotional patients leads to many treatments. Surgical measures are often recommended when some actual anatomical defect is present, or when the symptoms are considered the expression of organic disease.

The frequency of operations in this type of patient is shown in Table V.

TABLE V

SURGICAL OPERATIONS IN EMOTIONALISM

Females		Males	
Major	Minor	Major	Minor
29	59	5	5

Two patients had all the teeth extracted, and one had the uppers removed to cure the trouble. Forty patients did not have an

operation. The age periods in which operations were done are shown in Table VI.

TABLE VI

Decades	No. Patients	No. Patients Had Operations	No. Patients Without Operations
0-10	1	1	0
10-20	4	2	2
20-30	23	13	10
30-40	30	14	16
40-50	20	12	8
50-60	12	10	2
60-70	5	3	2

The cause of the disturbance in the eight patients not operated upon in the fourth decade was so obvious that an operation could not have been recommended. The same applies to the cases not subjected to surgery after fifty years of age.

Social Status

As sexual inhibition has enjoyed popularity in the etiology of this problem, the question was studied in all instances. The social status in this regard is given in Table VII.

TABLE VII

SOCIAL STATUS

Status	No. Patients
Single, young	21
Spinsters	9
Bachelors	4
Married	54
Widow	9
Widower	0
Divorced	1
Divorced, remarried	2

Anatomical Sites of Distress

Emotional patients usually have the greatest degree of distress in a particular organ or region of the body. The anatomical areas of distress as evidenced in the chief complaints of this group of patients are designated in Table VIII.

Precipitating Factor

The type of individual that is capable of emotionalism probably belongs to a definite biologic strain. Careful inquiries were made in each patient to determine the factor or factors underlying the complaints, which in many instances had existed for years. Other types of individuals with the same underlying factors do not develop emotionalism. The categories under which the precipitating cause could be classified are given in Table IX. There was rarely more than one important cause.

TABLE VIII

ANATOMICAL AREAS OF DISTRESS

Area of Distress	No. Patients
Heart	19
Abdomen	14
Stomach	29
Nervous system	34
Oesophagus, choking	3
Pains over body	2
Lungs	2
Liver	1
Blood pressure	2
Thyroid	2

Results of Treatment

The purpose of carefully studying patients is to give them a new viewpoint, recondition their mental reflexes, and have them learn a system of interpreting their reactions to various external and internal stimuli. The cases of brief duration are often adjusted in a short time, whereas in instances where the condition has existed for a long period of time, the problem is more difficult, and may not be adjustable. In this group sixty-five patients were trained to successfully manage their problems, and how to deal with new ones when they arose. Many of the patients in this group were under observation for years, and the results could be reviewed. Six patients were not followed. Sixteen patients were partially well, but would have recurrences that were poorly managed. The basic precipitating factor at times could not be changed, and in other instances the patient had insufficient self discipline to follow suggestions that might have value. Thirteen patients, although followed for fairly long periods, were not helped. One of these had severe migraine, and she became highly emotional over the recurring attacks, feeling that she had been unfairly

treated in life. She had had abdominal operations to cure the headaches and had become decidedly unhappy over her trouble. One case was associated with a post-influenzal debility, and she could not be helped. Another patient became agitated over learning she had high blood pressure in the course of an annual examination. She could not be re-assured although she was well before she had learned of the hypertension. The agitation increased the pressure. At the end of six months of observation she developed a cerebral accident and died in a few days. One mother, who had lost two sons in World War I, continued to sit by the window and weep. She refused to leave the house, having no interest in social events. She remained the same for the two years of observation. The other nine patients could not accept any educational advice and were seeking for a more concrete reason for the trouble, as well as a quick solution of their problems.

TABLE IX

PRECIPITATING CAUSE

Cause	No. Patients
1. Death in family	24
2. Sickness in family	9
3. Fear	7
a. Disease	
(1) Tuberculosis	3
(2) Heart	1
(3) Cancer	1
(4) Disease in general	2
(5) Goiter	1
(6) Cirrhosis of liver	1
b. Food	1
c. Closed places	2
4. Domestic infelicity	
a. Husband at fault	
(1) Unreasonable	2
(2) Worked at night	1
(3) Out of work	1
(4) Excitable	1
(5) Not attentive	1
b. Wife at fault	
(1) Deceived husband in trifles	1
(2) Suspected of being unfaithful, proved to husband not true	1
(3) Tension over money	1
(4) Children by former marriage of husband—led to conflicts	1
5. Parents	
a. Mother	1
b. Father	1
c. Both	2
d. Grandmother	1
e. Mother-in-law	1
6. Worry	
a. Over children	3
b. Money	3
c. Home responsibilities	4
d. Missed menstruation	2
e. Broken off love affair	1
f. Marrying right girl	1
g. Business	3
h. Over other members of family	3
i. Union trouble	1
j. Thinks of self	1
k. Broken tibia and anxiety lest not able to work again	1
l. Fractured spine	1
m. Conflicts of business	1
n. Told high blood pressure	2
o. Nurse worrying over patient	1
p. Chronic fatigue	1
q. Son going into Navy or Army	4
r. School	3
7. Sudden fright	
a. Seeing woman faint	1
b. Accident in street	1
c. Child killed in street	1
d. Block in subway during strike	1
8. Persistent sensations from an experience	
a. Seeing a large fire	1
b. Pregnancy—gastric sensations	1
c. Upset by thoughts at communion; kept thinking of ideas that occurred at the time	
d. Once vomited when excited and repeated act subsequently	1
9. General debility	
a. Post-influenzal	1
10. Frustration	
a. Wanted to be an actor	1

Discussion

As one-third of all patients are suffering from misunderstood emotional reactions, the subject of emotionalism is of first importance in medical practice. Alertness to the frequency of this type of suffering prevents many errors of judgment. Most of the one hundred patients of this study were observed for years. Other members of the family were also patients. The opportunities to obtain accurate data were excellent.

Seventy-seven of the patients were females. Seventy-eight of the patients were between 20 and 50 years of age. This is the most active physical and mental period of life. Individuals with nervous systems capable of reacting intensely to stimuli will experience most frequently unpleasant reactions in this age period. During this interval wisdom is being acquired and the value of various endeavors in life established. In addition to external stimuli, individuals are disturbed by doubts and fears while acquiring wisdom and mental poise. The more active the mind, the more the individual is disturbed by episodes, the end results of which are unknown.

One reason for the more frequent occurrance of emotionalism in females is indicated in the occupation of the persons comprising this study. Forty-three percent

of the patients were housewives. The reactions of inexperienced persons in rearing children combined with the strain of childbearing and household duties are important factors in the development of an unsatisfactory emotional state. The noise and quarrels of the children keep the emotions of the mother more or less constantly disturbed. Sickness of the children adds to the picture. Problems over home economics also disturb the mental quietude of many housewives.

Emotionalism occurs in persons with all types of vocations. The sufferer cannot escape the reactions of his or her own biological nature by change of occupation. Emotionalism exists in the idle, the occupied, the poor, and the rich. The physician must deal with the individual first, teaching a suitable way of interpreting the reactions to various types of stimuli.

The change required is in the viewpoint and the interpretation of sensations. These methods were used and change of occupation was not recommended. Those patients who changed occupations of their own volition were rarely any better. Cultivating a sense of indifference to annoyances works far better. Patients were taught not to discuss their feelings with anyone, as each descriptive repetition of the sensations impressed the mind more deeply. When asked "How are you?," they were taught to reply, "Much better, thank you." By this method the patients were not influenced by the unwise remarks that form such an important part of the advice that most people feel inclined to give others who are complaining. Many people are kept ill by the tactless remarks of the family. The emotional states that occur in families from disputes can frequently be lessened by the person who suffers keeping quiet about petty annoyances and, when misunderstandings occur, say "I am sorry," while going on to something less disturbing.

The study of life histories of emotional patients shows that females (Table IV) have slightly more acute illnesses than males. There is no evidence to show that these illnesses, except in rare instances, are the conditioning factors for the emotional state. The fatigue that exists after an illness with too brief a period of convalescence is at times the premise on which the patient becomes conscious of unpleasant sensations that are of emotional origin.

The infrequency of significant physical or laboratory findings in the emotional type of patient with the terms used in my early experience often led together with the method of approach to the remark: "Then you think that there is nothing the matter with me." A brief discussion of emotions and the sensations associated with an emotional reaction should precede the report of the results of the physical and laboratory examinations. The patient can then be informed that the state is one of emotionalism without an organically diseased background. Patients can be led to understand that a sound physical body has emotional reactions. There are many ways of presenting the reports, and the approach must be correlated with the general cultural development of the patient. In some patients, their thoughts are so concerned about themselves that they cannot hear what they are being told. Others have so lost faith in everything that their attention may only be obtained by stressing possible improvement. The patients who cannot concentrate or follow a routine are the most trying. The time spent in taking the history furnishes the clues to the method for opening the first discussions with the patient.

There is an emotional state with most organic diseases, but the method of approach is entirely different under such circumstances. In some instances the emotional state occurs after learning of an organic illness, and aggravates the organic disease. This is particularly true in some cases of hypertension, and is illustrated in this group by the woman who learned of her high blood pressure in the course of an annual examination.

Presentation of information concerning physical defects in a person who is recognized to be emotionally highly reactive should be done with the greatest care. Knowledge of unimportant physical changes often makes the primary condition worse, and the physician hampers his own

success by giving such details to the patient. The physical defects in patients under my care were never stressed, and, in fact, rarely mentioned directly. The indications that a variety of diseases might be considered were not mentioned. Every examination to exclude organic disease was done as indicated without presenting a group of reasons. Notes were kept of the possibilities from a pathologic standpoint, and, during revisits, the possibilities were checked. Revisits have significance and inspiration to emotional patients if repeated physical examinations are made, as the patient's fears are allayed by the knowledge that the body is being watched.

While re-examining the part of the body where the most distressing sensations occurred, it was my habit to say quite casually, "The heart is normal," "The abdomen shows no abnormal findings," etc. By using methods of brief reassurance during the revisit examinations, the mind of the patient becomes receptive to physiological and cultural advice in small instalments. In many instances considerable time, is required before highly emotional persons will hear in their minds the advice given.

Medical practice offers a suitable field for exploiting the unimportant physical findings in emotional patients. In early life the patient is willing to submit to surgical procedures that are not curative. This is shown in Tables V and VI. Sixty patients had ninety-six operations of which thirty-four were major procedures. None of the patients were cured by the surgical procedures. A surgical operation should never be recommended to cure an emotional state. If emotionalism exists in a patient who also has a disease that can be cured by surgical procedures, the patient should be told what complaints will not be present after the operation.

As indicated in Table VIII, the organic reference of symptoms in emotionalism prepares a background, which leads many patients into continuous trouble. They believe the trouble is located in a particular organ, and this belief is readily abetted unless words are carefully chosen. On account of the organic reference of symptoms many fallacious treatments are recommended and examinations made for which there are no basic indications. The best results with such patients are obtained through discussions to prove the normal state of the organ suspected. As many organic diseases are incurable, patients are helped by stressing that they are better off by being annoyed by normal sensations than if they were experiencing the symptoms of the disease suspected.

Sexual inhibition is often stressed as a basic cause of emotionalism. The possibilities for sexual gratification are presented in Table VII, which mentions the social status of the patients. There were thirty-four unmarried persons in the group. The four bachelors had all experienced complete sexual lives. There were twenty-one young persons who had not had sexual relations. The nine spinsters were virgins. In no instance in the 100 cases was sexual dissatisfaction brought out as a subject of importance in creating the emotionalism. In the instances where domestic infelicity existed, the disturbing factors were other than sex. Money, ignorance of etiquette, worry over sickness, problems with children, lack of confidence, and disputes about home management were the causes of the maladjustments.

The precipitating or basic factors were divided into ten types. The most cases were included under the general term "worry," which really means anxiety concerning the future. There were thirty-six cases that fell into this category. They included the common experiences of life. Some persons accept them without reaction, some as inevitable with a viewpoint that does not upset the peace of mind, whereas the group that becomes ill over the trials of life spends much time trying to solve the problem by escape or other activities. Most of these patients can be helped unless there is an unchangeable unsatisfactory condition in the home. True social service is guided in these patients by the causal factor or factors.

The second common cause of prolonged emotionalism was the reaction to death in the family or of a friend. In some instances the fatality had occurred after a prolonged illness. Some of the patients

had their sympoms referred to the same organ as the one affected in the family member who died. The two patients with headaches who believed the pain was due to a brain tumor were difficult to convince that their distress was emotional in origin. The suffering of the deceased member of their family had deeply impressed them. They both recovered after many revisits and examinations.

Clearly recognized fear was the cause in eleven cases. The fear of disease was the most common cause. Careful studies were required to convince the patients that the feared disease did not exist. There is a large element of fear in patients made ill by death in the family, as grief and fear are intermingled in such cases. There are very few patients with a fear state that can be helped by an abrupt frontal attack. That method was used in the woman who feared and believed that she had cirrhosis of the liver for twelve years. The advice was given after a week of intensive study in the hospital. She recovered promptly and resumed the management of her home.

The sensations brought on by a sudden fright produce a type of illness similar to the cases where the causal factor is less obvious. These sensations recur after the primary episode. The number of fear cases is increased by the inclusion of a variety of circumstances that may start the reactions.

Domestic lack of harmony was responsible for the ill health of nine cases. The causes of the discord varied, but cover in a general way the usual causes for domestic infelicity. In no instance was sexual incompatibility found to be the cause of the trouble, and the exploration of patients by chemical narcosis did not show any different data in this regard than obtained by the ordinary interview.

A post-influenzal state was the cause of the general debility with an emotional complex in one case. There were many of these cases after the epidemic of 1917. One patient's emotionalism was caused by his failure to make progress in his preparation to become an actor. The patient developed marked acne, which complicated his aims. After one year of illness, he was willing to change his social goal and gradually became adjusted in the preparation for a vocation to which he was better adapted. Frustration cases include those created by attempts at domination by members of the family. Many of these patients can be made well if the condition has not persisted over a long period.

In all types of emotional cases there is the element of fear. The patient looks too far into the future. I taught patients to practice what I dubbed "Divine selfishness." As long as the patient could not harm another by indifference, the aim was to interpret whatever occurred in life in such a way as to leave a comfortable state of mind. Furthermore, it was impressed that each individual must bear his own burdens, and that there was no value in thinking of consequences that usually never occurred. No one knows what is next in life, so why anticipate? To expect nothing leaves no chance of disappointment. The devout teachings of religion are a great help to those who fear what is ahead, and all those who showed interest in religion were encouraged to accept the comforts offered from undivided faith. The sources of the doctor's knowledge and experience are exploited to their uttermost by emotional patients. The wider the sources and experience are, the greater the opportunity to train this type of patient to live a reasonably satisfactory life.

The educational program with emotional patients begins as soon as the patient accepts the diagnosis. Much tact is required in dealing with the patients who have been ill for years and believe sincerely that they have organic disease. The advice given depends upon the knowledge of the examining doctor, and the more widely read he is and the more diversified his interests, the more likelihood he has of giving some understanding of the problem to the patient. The best books I found in dealing with the educated, fairly cultured patients are (1) As a Man Thinketh by James Allen, (2) The Open Door by Hugh Black, (3) The first chapter in Bliss Carmen's book, The Kinship of Nature. There are many valuable ideas in these books,

and nothing that conflicts with the religious concepts of people. These books furnish a medium of relationship between doctor and patient. Many other books may be used later. No books were recommended to uneducated people. They were more readily reached by speaking a language that they understood.

The technic used with people who were afraid of closed places, as subways, rooms, elevators, etc., was simple. The patients were instructed to memorize poems and, when they got into an unpleasant place, to repeatedly recite the poem to themselves as rapidly as possible. They would forget their surroundings while thinking of the poem, and the situation would soon change. Repetition of the test soon gave confidence, and the sufferer was self-convinced that the fear was groundless. This method in the course of years enabled a goodly group to overcome claustrophobia.

The fear of death, which becomes distressing to many people over thirty years of age, can be overcome by discussion with most people. The patient is reminded that the remembered experiences of life are the ones that disturb or please the consciousness. When patients clearly see that because there could be no remembered experience about death, therefore they could never suffer by death, the fear loses its significance. Individuals come into the world without remembered experience and the same applies to death. The least developed mentally can see that it is useless to be afraid of death in the light of the facts. It is the fear of death that in all probability underlies all cases that worry over sickness, or who become ill after members of the family die. In older patients in whom I knew this fear existed, as they left my office, in some casual way I reminded them that there was no danger of not continuing on life's journey.

Summary

1. 100 cases of emotionalism are presented.
2. The subject is discussed in a general and a specific way.
3. The results of treatment and its general outline are given.

1375 East 23rd Street

ENDOLARYNGEAL OPERATION

—Concluded from page 321

this one from me and I am sure no one shall be disappointed.

101 East 74th Street

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New Source of Rutin

According to a report by Dr. J. W. E. Harrison on May 3, 1950 at the American Pharmaceutical Association Convention in Atlantic City, N. J. a new source of rutin will substantially reduce the cost of medication with substances having vitamin P activity. Currently rutin is obtained principally from buckwheat which provides a yield of about 3 per cent of its weight. The new source reported, the flower buds of *Sophora japonica*, provides a yield of about 22 per cent of its weight. The tree from which these flower buds are obtained is popularly known as the "Pagoda Tree," and is cultivated for ornamental purposes in China. The author stated that, when properly purified, the rutins obtained from these two sources are identical chemically, physically, and toxicologically. Thus patients suffering with capillary fragility have the promise of less expensive and more readily available medication.

Aphorisms

Neurological Truths and Concepts

Andrew M. Babey, M.D.
Brooklyn, N. Y.

1. "—You must be dead sure before you speak. Give no kind of diagnosis before you are sure, for once you have spoken you cannot go back. There must be no subsequent examinations after the diagnosis (of neurosis) has been given, for no one believes in a vacillator. To go back and re-examine after the diagnosis will only make the patient think that you are not sure. He will not be reassured, only unsettled. He may often tempt you to re-examine, but do not yield. A man slow to make up his mind because he leaves no stone unturned is admired by patients, but a man who speaks because he is in a hurry to show how clever he is, and then changes his mind, will get nowhere with them."—T. A. Ross, *Edinburgh Med. J.*, May 1939, p. 318.

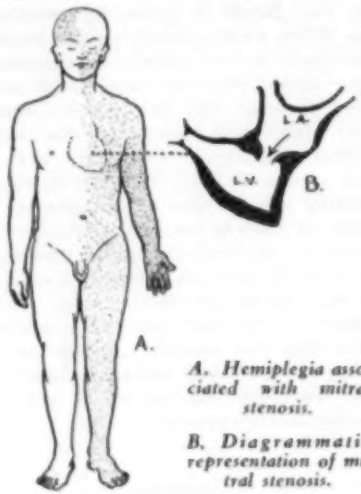
2. "—there is no question that alcohol alone can produce convulsions which are just like epileptic or uremic or paretic convulsions." Richard Cabot, *Case Records of M. G. H.*, March 27, 1923, #9132.

3. "Neuritis is one of the blinds behind which we try to hide our ignorance. In ninety-nine cases out of a hundred it is wrong."—Richard Cabot, *Case Records of M. G. H.*, May 1923, #9182.

4. "The 'blue line' of lead poisoning is not blue but black and not a line but dots of lead in the gums."—Richard Cabot, *Case Records of M. G. H.*, July 3, 1923, #9271.

5. "That old sign of picking at the bed clothes, what is called carphologia, used to be taught in textbooks as a sign of typhoid fever. I do not think we should say so now. It is a sign of chronic fevers with delirium in children or adults, but not particularly indicative of typhoid."—Richard Cabot, *Case Records of M. G. H.*, #9022.

6. "Hemiplegia is a very common complication of mitral stenosis, and in a younger person where it often occurs, it carries the best prognosis of any variety of hemiplegia that we know."—Richard Cabot, *Case Records of M. G. H.*, Jan. 10, 1922.



A. Hemiplegia associated with mitral stenosis.

B. Diagrammatic representation of mitral stenosis.

Dr. Babey, one time Bowen scholar of the New York Academy of Medicine (research Guy's Hospital, London) is now attached to the attending staffs of the Brooklyn and Kings County hospitals and to the teaching body of the Long Island College of Medicine, now a division of the University of the State of New York, and is the editor of this journal's Book News.

Editor's Note: From a vast field of medical literature Dr. Babey has garnered the most striking findings and the wisdom of a galaxy of experienced clinicians. They are arranged under the following headings: Cardiovascular (with which we opened the series in the April issue), Chest (which appeared in the May issue), Genito-Urinary (which appeared in the June issue), Nervous (which we are presenting here), Genito-Urinary, Gastro-Intestinal Tract, Blood, Thyroid, and Miscellaneous. They constitute for the practitioner a comprehensive post-graduate course whose value can hardly be overestimated.

7. "Meningitis patients are often hyperesthetic all over."—Richard Cabot.

8. "I have never seen an anterior bowing due to syphilis where the cortex was thin. There is generally marked thickening."—Richard Cabot, *Case Records of M. G. H.*, April 24, 1923, #9173.

9. "Any patient with Tertian or Quartan fever with skin eruptions and joint pains should be suspected of chronic meningococcemia."—C. Keefer, Ward Rounds, 1940.

10. "It is rare for signs of rib pressure (from cervical rib) to begin after the age of 30."—W. Harris, *Neuritis & Neuralgia*, Oxford Univ. Press, 1926, p. 82.

11. "Pain in genuine sciatica never comes round to the front of the thigh and groin, and when such pain is complained of it is usually due to some form of arthritis of the hip-joint or to anterior crural nerve disease."—W. Harris, *op. cit.*, p. 122.

12. "So uncommon is it for bilateral neuralgic pains in the lower extremities to be due to genuine sciatica that one should always look carefully first for any signs of polyneuritis, bone disease, pelvic tumour or central spinal disease such as tabes or spinal growth."—W. Harris, *op. cit.*, p. 122.

13. "The loss of an Achilles jerk is a useful proof of a neuritis of the sciatic nerve and may be a valuable point in differentiating this pain from other neuralgias of the limb such as arthritis of the hip-joint or anterior crural neuritis."—W. Harris, *op. cit.*, p. 127.

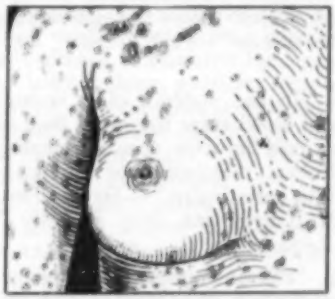
14. "One of the commonest types of psychalgia affecting the head is the well-known vertical pressure pain, like a weight pressing down on the top of the head. This pressure pain is usually worse in the morning, and is characteristic of neurasthenic depression."—W. Harris, *op. cit.*, p. 139.

15. "Dental neuralgia is never reflected across the middle line, a fact which appears to be insufficiently appreciated by practitioners."—W. Harris, *op. cit.*, p. 140.

16. "Pain referred to the ear and commencing in the ear and spreading forwards along the side of the cheek and into the lower jaw and neck, even sometimes to the shoulder and down the arm to the fingers, is highly suggestive of a lower molar tooth as the cause."—W. Harris, *op. cit.*, p. 171.

17. "Local tenderness on pressure or percussion of the spine is often a very prominent symptom in neurasthenia, known as neurasthenic spine; but in this case mobility of the spinal column is always normal."—W. Harris, *Neuritis & Neuralgia*, Oxford Press, 1926, p. 388.

18. "It has been shown from statistical studies that the highest studies of cures (of syphilis) occur in cases in which a 'secondary eruption' has been present."—Paul

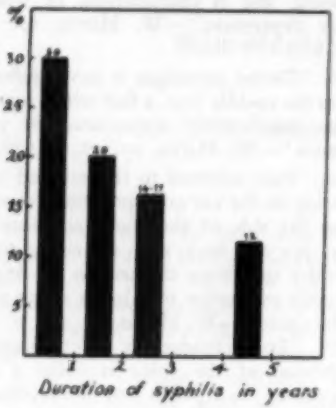


Secondary eruption of syphilis (maculopapular type).

O'Leary, *Proc. Interst, Post Grad. Assoc. N. Amer.*, 1941, p. 3.

19. "Examination of the cerebrospinal fluid will disclose involvement of the central nervous system in approximately 30 per cent of the cases in which syphilis has

been present for one year, in 20 per cent of the cases in which it has been present for 2 years, and in about 16-17 per cent of the cases in which it has been present for 3 years, and in about 12 per cent of cases



Percentage of involvement by years of the central nervous system in syphilis.

in which it has been present for 5 years." —Paul O'Leary, *loc. cit.*, p. 6.

20. "It is known that practically all of the malignant manifestations of syphilis become evident before the eighteenth year of the disease."—Paul O'Leary, *loc. cit.* p. 6.

21. "In the presence of a normal or elevated blood sugar the spinal fluid sugar is low only in acute purulent meningitis, tuberculous meningitis, or rarely acute syphilitic meningitis."—Frank Fremont Smith, *Boston Med. Surg. J.* 1925—Vol. 193:P.643.

22. "Human beings should gaily acknowledge their shortcomings. They should be taught neither to overcompensate for them nor to brush them out of consciousness . . . The ideal of general efficiency and of striving to be blameless is a wrong one . . . There is no reason to believe that there is only one fundamental problem lying at the base of neuroses . . . Modern men suffer from the idea that they should be perfect . . . Parents have to pay dearly for every perfectionistic ideal they put into their children's minds."—Vernon P. Williams, M.D., *New England Jour. of Medicine*, Mar. 14, 1940.

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Toxicity of Vitamin B_{12}

Forty white mice having an average weight of 11 Gm. received 7.5, 15, or 39 micrograms of vitamin B_{12} intraperitoneally or 30 micrograms subcutaneously. None of the mice died from the 7.5 microgram dose but 2 of 10 died with the 15 microgram dose. The 30 microgram dose was lethal to all of the mice. Traina, reporting in *Arch. Path.* [49:278 (Mar. 1950)] stated that the only pathological finding was congestion and edema of the lungs and slight congestion of the viscera. In another series 12 guinea pigs were given 5 micrograms of vitamin B_{12} subcutaneously daily for 21 days followed by 15 micrograms intraperitoneally after an interval of 37 days. There were no immediate or subsequent reactions in any of these animals with an average weight of 400 Gm.

Alpha Tocopherol in Heart Disease

Alpha-tocopherol was administered orally to 19 patients with chest pain ranging from 2½ months to 15 years duration who had either arteriosclerotic or hypertensive heart disease or both. Placebos were given to 19 similar patients. Travell *et al*, writing in *Ann. N. Y. Acad. Sci.* [52:345 Oct. 31, 1949)], stated that the treated patients received 200 mg. α-tocopherol acetate a day for 2 weeks and then 100 mg. three times a day for 10 to 20 weeks. The response was essentially the same in the two groups of patients for 12 treated and 14 control subjects showed no improvement and 7 treated and 5 control subjects reported partial relief of pain. Only 2 patients showed improvement in exercise tolerance when tested by examiners unaware of the type of medication given. Both of these were in the control group.

EDITORIALS

The Discovery of Ether

Sulphuric ether was discovered in 1540 by a young German student in Italy; he was Valerius Cordus, son of a physician, Euricius Cordus. He learned that brandy was called aqua vitae and sulphuric acid was called oleum vitae. He concluded that upon pouring the water of life into the oil of life and distilling the whole mixture something particular—maybe the oil of eternal life—might result.

The product was ether. While he was trying out its medical uses he died in Rome at the age of twenty-nine. Therefore humanity had to wait 300 years until ether was used for narcosis in 1844.

Valerius Cordus (1515-44) was an accomplished botanist who described about 500 new plants. His Dispensatorium was the first real pharmacopeia to be published (Nuremberg, 1535). M. W. T.

Edward Turner, Forgotten Pioneer in the Field of Alcoholism

Large corporations now recognize alcoholism among their employees as a disease which is one of theirs and the nation's most serious public health problems, accounting for a vast amount of absenteeism (28,000,000 work-days), lowered productivity and accident losses. They are providing medical and psychiatric facilities to cope with it through their own medical departments and other agencies.

The central fact in this matter is the recognition of compulsive drinking as a disease. The work of the Yale Laboratory of Applied Physiology and of Rutgers University has led to the conception of the alcoholic as a sick person. There are about 4,000,000 problem drinkers in the country, of whom 750,000 are classified as chronic alcoholics with impaired physical and mental health. It is estimated that three persons out of every 100 employed drink enough to be classed as alcoholics. The economic loss runs to $1,000,000,000 annually.

In view of the prevailing conception of alcoholism as a disease, it is interesting to recall the futile efforts of Dr. Edward Turner, founder of the Inebriate Asylum at Binghamton, New York, to establish this view of the condition. That was his basic tenet. He was destroyed by implacable proponents of a moralistic conception of the problem.

Biographic sketches of Turner were written by C. H. Shepard (1889) and by T. D. Crothers (1889). Turner himself wrote *A History of the First Inebriate Asylum in the World* (1888).

Chain-Smoker's Hope

The remedy for alcoholism known as Antabuse works by producing a hypersensitivity to alcohol, so that after the ingestion of the latter flushing, giddiness, headache, accelerated and deepened respiration and pulse rate, nausea and vomiting, and sometimes convulsions, result. The feeling of discomfort is intense, and, once experienced, the patient makes no further attempt to drink alcohol as long as he is using Antabuse. To put it mildly, he develops an aversion to it.

Perhaps only some such principle will ever avail in the case of one of the most intractable of addictions—the cigarette habit; but it will have to be something worse than Antabuse—like being struck by lightning, we should say.

The habitué lights up, whereupon an atomic bomb-like explosion is duplicated.

Who would ever again reach for an Unlucky?

A fascinating domain of therapy seems to have been opened.

The Oslerian Tradition

We have been taken severely to task by the eminent editor of a contemporary journal for permitting a contributor to assert that Osler once advised the shooting of the aged.

The contributor, like many others, must have had in mind Osler's address, now to be found in the volume titled *Aequanimitas* (pages 382-383), in which he made the following remarks: "In that charming novel, *The Fixed Period*, Anthony Trollope discusses the practical advantages in modern life of . . . the admirable scheme of a college into which at sixty men retired for a year of contemplation before a peaceful departure by chloroform . . . The teacher's life should have three periods, study until twenty-five, investigation until forty, profession until sixty, at which age I would have him retired on a double allowance. Whether Anthony Trollope's suggestion of a college and chloroform should be carried out or not I have become a little dubious, as my own time is getting so short."

This editor accepts whatever responsibility is his in the circumstances, but he feels that the charge of "recklessly defaming Osler's character" is a harsh one to lie against any doctor, for the unbounded esteem in which Osler has been traditionally held by all of us is indeed a universal phenomenon, and this includes even your humble servant. It would be impossible in any case to defame such a character as Osler's.

Circuit Rider

In some of our early settlements, the circuit rider was an outstanding feature of a primitive society. The circuit was a district assigned to a preacher who traveled on horseback, baptizing, marrying, converting sinners, and conducting funerals where regions were too sparsely inhabited to build or support churches.

In connection with recent poliomyelitis investigations in Arkansas the public health authorities sent "circuit riders" on rounds three times a week, collecting important specimens for laboratory study from field workers.

Today's effort in such areas is thus an evangelizing of health, the advocacy of a gospel of life. The rites practiced have to do with immunization and the preaching of hygiene to sinners against the laws of health.

An interesting revival of a frontier method, with much the same aim—moral health in the community in the one case, physical health in the other.

But, after all, it is permissible to think of the official sanitary inspector working by auto for the health authorities or foundations in any district, urban or rural, as a glorified circuit rider propagandizing a faith.

Washington's Commendable Delousing Process

"Operation Delousing" seems to have begun auspiciously. Since our editorial discussion of "The Homosexual Factor in Fifth Columns," in the March issue of the MEDICAL TIMES, John E. Peurifoy, Deputy Under-Secretary of State in charge of the security program, testified as follows before the Senate appropriations subcommittee. Mr. Peurifoy conceded that eleven State Department employees whose discharge he had ordered had been allowed to resign.

"How many others," asked Senator Bridges, "have resigned under investigation?"

"Ninety-one persons in the shady category," replied Mr. Peurifoy. "Most of these were homosexuals."

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Schering Establishes Endocrine Research Fellowship

Another Research Fellowship in Endocrinology has been established at Rutgers University by Schering Corp. According to Dr. James H. Leathem, endocrinologist and staff member of the university's Bureau of Biological Research, the grant is intended for the support of fundamental research by graduate students in the field of steroid hormones.

CONTEMPORARY PROGRESS

MEDICINE

Malford W. Thewlis, M.D.*

Aureomycin in the Treatment of Influenza and Certain Other Acute Respiratory Infections With or Without Pneumonia

M. Finland and associates (*American Journal of Medicine*, 8:21, Jan. 1950) report the use of aureomycin in 41 cases of severe acute respiratory infection. In 18 of these cases, the infection was proved to be influenza A; in most of these cases there were clinical symptoms of bronchopulmonary infection, but pulmonary involvement was demonstrated by x-ray in only 7 cases. In 10 cases, the symptoms were very similar to those in the influenza cases; 3 of these were cases of nasopharyngitis and tonsillitis due to a beta hemolytic streptococcus, but no causative agent could be demonstrated in the other cases in this group and none had pneumonia. In 13 cases there were definite signs of pulmonary consolidation on physical examination, confirmed by x-ray, but the causative organism could not be determined. In all but one of these cases aureomycin was given by mouth in doses of 1.0 or 0.5 Gm. every four to six hours; when the patient's temperature reached normal and the general condition improved this dosage could be reduced. One patient was given aureomycin by intravenous injection without oral administration and 3 patients were given aureomycin intravenously or intramuscularly in addition to oral administration. In the first two groups, response to aureomycin therapy was prompt, with defervescence and relief of symptoms; in the cases with pulmonary lesions in the first group, these lesions cleared up promptly. In the third group, in 5 patients with clinical symptoms of lobar pneumonia, the response to aureomycin was also prompt. In the other 8 cases in this group in which pneumonia complicated some other condition, there was only temporary and partial improvement. The untoward effect of aureomycin given by mouth was some gastrointestinal disturbance, usually not sufficiently severe to interfere with continuation of the therapy; occasionally the dosage had to be reduced. Intramuscular administration caused pain. One intravenous injection was followed by a pyrogenic reaction, and one by a small area of cellulitis. There was no evidence of a toxic effect of aureomycin on the kidneys, blood forming organs or nervous system.

COMMENT

Aureomycin evidently is the answer to the problem of many virus infections. I am impressed with the good results from 250 mg. daily in mild infections. Naturally severe infections require larger amounts. There is reason to believe that in ordinary infections smaller doses once a day elevate the blood level of aureomycin satisfactorily ***M.W.T.***

Tetraethylammonium Chloride in the Treatment of Angina Pectoris

W. J. Atkinson, Jr. (*American Heart Journal* 39:336, March 1950) reports the treatment of 28 cases of angina pectoris with tetraethylammonium chloride. All the patients were clinic patients and came to the clinic for treatments. Tetraethylammonium chloride was given by intravenous injection, beginning with small doses (50 or 100 mg.), and gradually increasing until the optimum dose for each patient was found. It was always given with the patient lying down, and the patient was not allowed to sit or stand up until the blood pressure returned to normal range. In most cases treatments were given once every one or two weeks; in some of the most severe cases injections were given twice a week until there was definite improvement. Occasionally during periods when attacks were severe a patient would be hospitalized for a time and given treatment every one or two days. Of the 28 patients treated, 25 have shown definite improvement in decrease of the number of attacks and an increase in exercise tolerance. Status anginosus and persistent long-continued aching pain and discomfort associated with coronary insufficiency were relieved in those cases in which these symptoms were present. Sixty-five per cent of the patients in this series have been under

*Diplomate of American Board of Otolaryngology; attending staffs St. Anthony and State University Hospitals; Associate Professor of Otolaryngology, Oklahoma University.

treatment for six months and longer, and none have shown any ill effects although 65 per cent were over sixty years of age, and 70 per cent had had a myocardial infarct or congestive failure before the treatment was begun. No conclusions are drawn as to beneficial effects of the treatment other than symptomatic improvement, but the relief of symptoms obtained in many of the cases was "most gratifying."

COMMENT

There have been many reports of excellent results in angina pectoris from placebos. It will be interesting to have many more experiments with tetraethylammonium chloride before forming definite conclusions M.W.T.

Dicumarol Prophylaxis of Thromboembolic Disease in Congestive Heart Failure

W. P. Harvey and C. A. Finch (*New England Journal of Medicine*, 242:208, Feb. 9, 1950) report a study of 180 patients with congestive heart failure, 80 of whom were given Dicumarol, the other 100 serving as a control group. The two groups were similar in respect to age, types and severity of the cardiac disease. Daily prothrombin determinations were made while Dicumarol was being used, and the dosage was calculated to maintain prothrombin time at approximately 30 per cent. At first Dicumarol was given only to patients whose prothrombin time before beginning therapy was over 60 per cent, but later patients with lower prothrombin levels were also treated. During the period of observation all these patients were hospitalized, and only complications thought to occur during the period of hospitalization were considered. During this period pulmonary emboli occurred in 13 of the 100 patients in the control group (8 proved at autopsy); there were also 2 questionable cases of pulmonary emboli in this group. In the group of 80 Dicumarol-treated patients, there were only 2 questionable cases of pulmonary emboli. Thrombophlebitis was a complication in 8 cases of the control group; in the Dicumarol-treated group, there was one definite and one questionable case of thrombophlebitis. The mortality rate in the control group during hospitalization was 17 per cent, in the Dicumarol-treated group, 9 per cent. Of the 17 deaths in the control group, 8 were due to pulmonary embolism, while there was no case of fatal pulmonary embolism in the Dicumarol-treated group. These findings indicate that treatment with Dicumarol results in a "significant reduction" of thromboembolic complications in congestive failure, and thus in a decrease in the mortality of hospitalized patients.

COMMENT

No doubt about the efficacy of dicumarol in the treatment of congestive failure. This also applies to the treatment of coronary thrombosis. Careful supervision of treatment is required. It is interesting to note that the results with older methods of treatment have proven almost as satisfactory as the newer approach. M.W.T.

The Treatment of Capillary Fragility with a Combination of Hesperidin and Vitamin C

G. J. V. Solsman and S. Horoschak (*American Journal of Digestive Diseases*, 17:92, March 1950) report the treatment of 38 patients showing evidence of capillary fragility with a preparation combining hesperidin (vitamin P) with ascorbic acid, known as Hesperidin-C. All these patients showed petechiae, ecchymosis, or purpura and all gave positive reaction to the capillary fragility test. The underlying disease in these cases,, chiefly hypertension, arteriosclerosis or arthritis, was treated by the generally accepted medical measures. Hesperidin-C was given by mouth; at first three tablets (hesperidin 50 mg. and absorbic acid 50 mg.) were given four times daily; after six weeks eight tablets were given daily in divided doses for another six weeks; when the capillary fragility test showed normal capillary resistance, four tablets daily were given as a maintenance dose. In the majority of the patients, the treatment was successful in maintaining normal or nearly normal capillary resistance and in relieving the symptoms due to capillary fragility. In 9 patients whose capillary fragility tests had been normal for six months, and who showed no tendency to spontaneous petechiae, ecchymoses or purpura, Hesperidin-C therapy was discontinued; 7 of these patients developed clinical evidence of increasing capillary fragility and positive reaction to the test, which were again corrected by returning the patients to maintenance doses of Hesperidin-C.

COMMENT

I have been using Hesperidin-C routinely in all hypertensive patients who show capillary fragility. Thus far I am convinced that those who take this treatment have fewer vascular accidents than those who disregard the signal. However, the tests for capillary fragility are not always accurate; therefore, it might be well to use this preparation routinely in all hypertensive patients. M.W.T.

The Use of ACTH and Cortisone in Neoplastic Disease

O. H. Pearson and associates (*Bulletin of The New York Academy of Medicine*, 26:235, April 1950) state that a previous report showed that the administration of ACTH or cortisone acetate induced a temporary regression of lymph node and splenic enlargement in 4 patients with chronic lymphatic leukemia, one patient with follicular lymphosarcoma, and one with Hodgkin's disease. In all these cases a regrowth of the tumor masses was evident in ten days to three months after treatment was stopped; 3 of the patients, 2 with chronic leukemia and one with lymphosarcoma, showed a satisfactory response to a second course of treatment. More recently ACTH has been used in the treatment of 5 cases of acute leukemia not previously treated, 3 children and 2 adults; 4 of these 5 patients had acute granulocytic leukemia and one (a child) had acute lymphatic leukemia. ACTH was given in doses of 50 mg. daily for the children and 100 mg. daily for the adults for twenty-four to thirty days. All these patients showed a definite remission—regression of the enlarged lymph nodes, cessation of bleeding, improvement in the general condition, and improvement in the blood picture with increased maturity of white bloodcells and return of the white cell count to normal, a reticulocyte response and increase in platelets. While there was a definite improvement in the bone marrow, with increased maturity of the myeloid cells, abnormal cells did not disappear entirely either from the bone marrow or the blood. One of the children had been in remission for five weeks at the time of the report; another child had a recurrence of symptoms within three weeks, but showed symptomatic improvement when ACTH was again given. In the other 3 patients, the period of observation since discontinuing treatment did not exceed sixteen days at the time of this report. Two children with acute luekemia were given ACTH after having been treated with folic acid antagonists; one died in two days with an intercurrent infection; the other, who was critically ill, showed some symptomatic improvement, but died in fifteen days. Cortisone has been tried in only 2 cases of acute leukemia, both in children; one showed a good remission; the other died within forty-eight hours after beginning therapy. While remissions can be obtained with ACTH in most cases of acute leukemia, these remissions are "both incomplete and temporary." ACTH and cortisone have been used in a few cases of malignant tumors of various types, including carcinoma, without definite effect on the growth of the tumor.

COMMENT

Unfortunately, this treatment is of benefit only to children. For adults, lymphocytic leukemia is best treated—at the moment—by roentgen rays. ***M.W.T.***

OTOLOGY

L. Chester McHenry, M.D., F.A.C.S.

Suggestions for Determining the Mobility of the Stapes by Means of an Endotoscope for the Middle Ear

G. V. Békésy (*Laryngoscope*, 60:97, Jan. 1950) describes an instrument which has been used for the measurement of transmission in postmortem studies. If the patient's degree of hearing loss is known, and it is possible to measure the conduction loss postmortem by this instrument, the difference between the two values measures the nerve deafness. Both the conduction loss and the nerve loss can be expressed in decibels. In postmortem studies, this makes it possible to determine the importance of various histological findings in the causation of transmission deafness and nerve deafness. In a study of 4 cases of otosclerosis, comparison of the conductive loss at 1000 cps. with the mobility of the stapes measured by static pressure indicated that it would be possible to predict conductive loss for tones, if there is an observable stapes fixation under static pressure. A small endotoscope has been constructed, which can be introduced through a small perforation in the eardrum, and with which mobility of the stapes can be observed. This instrument has proved valuable in animal experiments for the examination of the ear canals, and later it will be used in the examination of patients, especially for the determination of the mobility of the stapes as an aid in the diagnosis of causes of loss of hearing.

COMMENT

Useful in research. We doubt that the practical value to the hard-of-hearing patient

will be enough to induce his submission to such a procedure. *L.C.McH.*

The Plight of the Nerve-Deaf Patient

L. E. Morrissett (*Archives of Otolaryngology*, 51:1, Jan. 1950) reports that he has used the various methods of treatment advocated for nerve deafness, but that with an adequate follow-up, he has never had a patient with nerve deafness show any significant sustained improvement in hearing. Tinnitus may be diminished and has occasionally disappeared with some methods of treatment, especially with neostigmine given intramuscularly or with vitamin B. If vitamin therapy and other tonic therapy build up the general health of the patient and relieve fatigue, it may improve the hearing acuity by improving his alertness. If this conclusion, that nerve deafness is generally irreversible, is accepted, the only chance of readjustment to life for the person with nerve deafness lies in aural rehabilitation. Ample facilities for aural rehabilitation are provided for veterans through the Veterans Administration, but for other civilians such facilities are not generally available. Most hospitals and most otologists in private practice are not equipped to carry out an aural rehabilitation program. "Mass facilities" for such a program should be provided either by certain hospitals, particularly specialty hospitals in each community, or by the otologists of the community. Certain hospitals have already provided such facilities, such as the Hearing and Speech Center at Johns Hopkins Hospital, the hearing clinic at the Eye, Ear, Nose and Throat Hospital of New Orleans and an aural rehabilitation center at the Reading Hospital. Coordination of all activities is essential for aural rehabilitation. It should include provisions for a complete medical and otologic study of each patient, including audiometric tests, tests of auricular ability and similar tests, provision of hearing aid when indicated and training in the use of such an aid, auditory training for preservation of residual hearing and in the attention factor, training in lip reading. Psychologic care and psychiatric care are needed by many deafened patients; voice training and speech correction are indicated in some cases; and vocational guidance is also necessary for some patients. All these should be a part of the aural rehabilitation center. The otologist is "the focal point" in this program, but he needs the assistance of other specialists for carrying out the entire program.

COMMENT

Aural rehabilitation is a tremendous help to deafened patients and requires extensive resources in personnel and equipment. For initial diagnosis and treatment of anatomical lesions so far as is practicable the otologist is necessary. His primary value in these patients is to know that there are facilities for such rehabilitation and to help his patients by referral to such centers. *L.C.McH.*

Treatment of Recurrent Otitic Barotrauma by Irradiation

E. D. D. Dickson and J. E. G. McGibbon (*Journal of Laryngology and Otology*, 63:647, Nov. 1949) report a study of radiation therapy in recurrent otitic barotrauma in the air force. The inequality between the atmospheric and intratympanic pressures during flying or decompression or recompression in a chamber, which is the cause of otitis barotrauma, results from impaired patency of the lumen of the eustachian tube. Submucosal lymphoid tissue around the orifice of the eustachian tube is one of the factors that interferes with patency of the tube. Evidence has also been found that excessive subepithelial lymphoid tissue within the eustachian tube may also be a factor in diminishing its patency. While radium or radon in the nasopharynx is successfully used for the reduction of excessive lymphoid tissue around the orifice of the eustachian tube, it has been found that a safe dosage of radium or radon accurately positioned in the nasopharynx has little effect on lymphoid tissue in the walls of the eustachian tube. Hence a method of application of deep x-ray therapy has been worked out, based on measurements of the head of each patient, so that the dose levels to various tissue may be altered as required. This method of treatment was used in a series of 64 members of the air force who showed symptoms of recurrent otitic barotrauma and who were unable to auto-inflate the middle ear on the ground or in simulated flight, but who showed no evidence of previous middle ear infection, or nasal sinus disease and no lesion of the nasal fossae, nasopharynx and pharynx. With the method of x-ray therapy employed, three or four fields were used (according to the indication in each case) and all fields were irradiated daily for five days per week for ten treatments. At first the dosage employed was 100r to each field, which gave an average total dose to the eustachian tube of 1000r (ranging from 860 to 1,245r). Later a higher total average dose to the eustachian tube was employed, 1,380r (ranging from 1,250 to 1,520r). A patient was considered cured when he could undertake flying with no restriction as to height, and with no recurrence of symptoms. Of the 41 patients treated with the lower dosage, 15 or 36.3 per

cent were cured; of the 23 patients treated with the higher dosage, 13, or 56.5 per cent, were cured. Thus of the entire series of 64 patients, 28, or 43.7 per cent, were cured.

COMMENT

The value of radiation therapy of any type in the treatment of malfunction of the eustachian tubes lies in its effect upon lymphoid tissue which is interfering with function of the eustachian tubes. Extreme care in the use of such radiation is of primary importance. We suspect that the patients in this group who were "cured" had lymphoid tissue in their nasophraynges which was interfering with proper ventilation of their middle ears.

We are quite sure that the nasophryngeal radium applicator is being used in this country for many conditions which it is not designed to help. In another ten years we may be able to detect some of the untoward results of such unwise radiation in the nasopharynx. Those interested should read the discussion of this problem at the meeting of the American Academy of Ophthalmology and Otolaryngology in 1949. L.C.McH.

Use of Radium in the Middle Ear for Selected Cases of Chronic Otitis Media

W. W. Wilkerson, Jr. and associatrs *(Laryngoscope,* 59:1248, Nov. 1949) report the use of radium in the treatment of chronic otitis media complicated by the presence of chronic granulation tissue, polyps or fibroma in the middle ear. As such complications are comparatively rare in chronic otitis media, only a small series of cases, in which radium was considered to be indicated, is reported. The nasopharyngeal radium applicator was employed containing 50 mg. of radium; it was found that with this applicator, the 50 mg. of radium could be safely applied in the middle ear for ten to twelve minutes. In the 10 cases reported, the maximum dosage was four ten-minute treatments; in some of the cases only five-minute treatments were employed. Any polyp or fibroma was first removed surgically, as completely as possible, the radium applicator being applied to the base three to six days later. When treatment was repeated, the interval between treatments was thirty days. In 8 of the 10 cases reported, the results were good or excellent, the middle ear growth or granulations disappearing completely, and the lining membrane appearing normal or nearly so; in the 2 cases in which results were not satisfactory, the growths in the middle ear showed evidence of atrophy. The use of radiation in the middle ear in these cases is correlated with radiation therapy of similar tissues in other parts of the body.

COMMENT

The nasopharyngeal radium applicator is designed so that the radium is not placed in the tip of the applicator but several millimeters away from the tip. Its use in the external auditory meatus would result in tremendously greater dosage to the walls of the outer portion of the external meatus than to the middle ear areas against which the tip of the applicator was placed. It would be interesting to know what happens to the skin in these external meati in the years to come. L.C.McH.

Lightning as a Cause of Hearing Loss

G. Brooks West, Jr. *(Laryngoscope,* 59:1350, Dec, 1949) presents a review of the literature on injuries to the ear caused by lightning and reports a case in which a unilateral loss of hearing was the only injury caused by a lightning stroke. In one case reported in the literature, a fracture of the skull due to lightning was associated with burns and injury to the ears with loss of hearing; in one case, deafness was unilateral and was associated with bleeding from the ear, although inspection of the drum after the bleeding stopped showed no evidence of trauma to the ear drum or canal; in another case, there was slight bleeding from both ears, without perforation of either drum, but the umbo and its surrounding area were congested and ecchymotic six days after the injury. In the author's case the patient was a man thirty years of age who was exposed to a bolt of lightning that killed a boy standing near to him. On recovering from the shock of the accident, the patient noted loss of hearing and "a roaring noise" in the right ear. Examination showed the ear drum of this ear to be intact but markedly injected; an audiogram showed a nerve type hearing loss. Hearing began to improve within a few days and when the patient was examined nine months later, the hearing was practically normal; both ear drums were in good position and of normal color. In this case, the hearing loss was probably due to an edematous process, with or without hemorrhage, involving the cochlea or auditory nerve, or possibly the hearing cortex. The almost complete recovery of hearing indicates that there was no direct electrical injury to any of these structures.

COMMENT

Sounds like a temporary traumatic deafness. L.C.McH.

RHINOLARYNGOLOGY

L. Chester McHenry, M.D., F.A.C.S.

Cardiovascular Epistaxis and the Naso-Nasopharyngeal Plexus

G. H. Woodruff (*Laryngoscope*, 59:1238, Nov. 1949) reports 28 cases of cardiovascular epistaxis, which he distinguishes from the ordinary type of epistaxis in which the bleeding comes from Kiesselbach's area—sometimes called epistaxis digitorum. The latter type of epistaxis occurs usually in children and young adults and is not associated with hypertension. Cardiovascular epistaxis occurs in patients of middle age and older with definite hypertension; the youngest patient in the author's series of 28 cases was forty-one years of age. The location of the bleeding site in cardiovascular epistaxis is usually outside Kiesselbach's area. The most frequent site is in the lateral wall of the inferior meatus far back; this was the bleeding site in 14 of the author's cases. Other bleeding sites in these cases were the septum just above and posterior to Kiesselbach's area, an area high up and far back in the nasal cavity, the lateral wall in front of the middle turbinate, and Kiesselbach's area proper (in 3 cases). Examination of the nasal cavity with the nasopharyngoscope in patients who had cardiovascular epistaxis and in others, showed that there is, in many persons, a group of blood vessels in the lateral wall of the inferior meatus well posteriorly, which come from the lateral pharyngeal wall; in young persons these blood vessels are small and not prominent, but in older persons, they are more numerous, larger, and often appear dilated. The appearance of these blood vessels indicates that they are veins, but probably arterial vessels accompany them at a slightly greater depth. This group of blood vessels has been designated by the author as the naso-nasopharyngeal plexus. In cardiovascular epistaxis the bleeding frequently comes from this plexus, either the veins or the arterial vessels that lie slightly below them. When the bleeding comes from Kiesselbach's area or some other anterior site that can be visualized and exactly localized, the electrocautery has proved effective in treatment. When the bleeding comes from the posterior portion of the lateral wall of the inferior meatus, and the site of the bleeding cannot be exactly located, electrocauterization is difficult without destroying uninvolved mucous membrane. In these cases the author prefers to use a special method of tamponage, in which several tampons are used to fill the interior meatus and exert firm pressure on the posterior portion of the lateral wall. Before the tampons are introduced a small amount of 4 per cent aqueous solution of tannic acid is added to a similar amount of 4 per cent aqueous solution of antipyrine, causing "a rubbery precipitation" into which each tampon is plunged before being inserted, except the last tampon that holds the others in place. The tampons are left in for five days, by which time healing usually takes place. In cases where bleeding can not be controlled by other methods, ligation of the external carotid artery is indicated. This was done in 4 of the author's cases, in 3 of which a deflected septum made it difficult to use tamponage effectively.

COMMENT

Epistaxis can be extremely difficult to control in such cases. In addition to local measures, such as the author outlines, the administration of morphine in sufficient dosage to maintain its physiologic effect over several days has been extremely useful. *L.C.McH.*

The Effect of Nasal and Sinus Surgery Upon the Manifestations of Allergy

F. L. Weille (*New England Journal of Medicine*, 242:43, Jan. 12, 1950) discusses the value of nasal and sinus surgery in asthma and vasomotor rhinitis on the basis of a study of 783 cases of asthma, vasomotor rhinitis or both, previously reported; 276 cases of surgical frontal-sinus cases (only 10 with asthma); and other groups of cases, mostly not previously reported, including 272 surgical cases of vasomotor rhinitis (51 of these patients also had asthma); and 255 surgical asthma cases (including these 51 cases). In both asthma and vasomotor rhinitis the local nasal condition was improved by surgery in about 75 per cent of cases. There was improvement in the symptoms of asthma after nasal or sinus surgery in about 50 per cent of cases of intrinsic asthma, reflex asthma and extrinsic infective asthma. Surgical procedures that improve the mechanical and physiological state of the nasal cavities, and lessen the sinusitis in the antrum, ethmoid and sphenoid sinuses give better local results in the nose and sinuses and as good a degree of improvement in the symptoms of vasomotor rhinitis and asthma as more radical

external operations in the ethmoid and sphenoid sinuses. At present, it has been found impossible to determine preoperatively which patient with vasomotor rhinitis or asthma will be benefited by surgery; study of final results may, however, indicate more definitely the indications for surgery in these cases. It is suggested that "a specific allergy virus" or nasal viral infection may be the cause of nasal and sinus polyposis, vasomotor rhinitis and intrinsic asthma, and that this possibility is "an attractive field" for research.

COMMENT

Sinus surgery, exactly like other major surgery, gives satisfactory results when it is used to "improve the mechanical and physiological state of the nasal cavities." There is no other excuse for the performance of sinus surgery and benefit in cases of asthma can be expected only when the condition of the nasal cavities themselves warrants sinus surgery. L.C.McH

Procaine Penicillin Solution in the Treatment of Nasal Polypi

S. L. Ruskin *(Laryngoscope,* 60:111, Jan. 1950) reports the use of procaine penicillin solution in the treatment of chronic sinusitis and polyposis. For the preparation of the procaine penicillin solution, 20cc. of procaine ascorbate solution is added to a vial containing 100,000 units of sodium penicillin, forming procaine penicillin and sodium ascorbate. Or one of the commercially available suspension solutions of procaine penicillin may be used; 1cc. of such a solution, containing 300,000 units of penicillin, is diluted with 60cc. of sterile saline, and 10 cc. of this solution instilled into each antrum and 5 cc. into each sphenoid sinus. With procaine penicillin the rate of absorption of penicillin is so slow that when a solution of 3,000 to 5,000 units per cc. is instilled, it remains in the sinus for at least one to three days and sometimes for a week; this gives a large dosage of penicillin at the infected site. Another factor of benefit in the use of procaine penicillin is the antihistamine action of procaine, which aids the decongestion of the sinus and nasal mucosa. The author has found that with this treatment chronic sinus conditions of long standing show "striking" improvement and nasal polyps shrink rapidly and finally disappear. An illustrative case is reported in which chronic sinusitis and polyposis of twenty years' duration cleared up after repeated instillations of procaine penicillin, and there has been no recurrence in six months after completion of treatment.

COMMENT

We have had no experience with the use of procaine-penicillin locally in the sinuses. We have been disappointed in the use of other penicillin preparations locally on the nasal and sinus mucous membrane. We are also somewhat loath to use penicillin preparations locally in allergic noses (practically all polypoid noses are allergic) for fear of inducing sensitivity to pencillin. L.C.McH.

Laryngeal Polypoid Growths Following Endotracheal Anaesthesia

Ali El-Mofti *(Laryngoscope,* 63:759, Dec. 1949) reports 2 cases in which a polypoid growth of the larynx developed two months or more after operation under endotracheal anesthesia. In one case, the endotracheal tube was inserted by the blind nasal route after repeated attempts; in the other case, the tube was finally introduced by direct laryngoscopy after several attempts to introduce it through the nasal route had failed. In both cases the first symptom was hoarseness, beginning two to four months after operation; one patient also complained of aphonia during speech. Examination by indirect laryngoscopy showed a polypoid growth of the larynx, which in each case, was attached below the posterior end of the left vocal cord and the vocal process of the arytenoid. In the patient who had noted aphonia during speech the mass was seen to rise during phonation and was caught between the vocal cords. The growth was completely removed by indirect laryngoscopy in one case and by direct laryngoscopy in the other, with complete relief of symptoms. Histologically the growths showed the characteristics of organizing hematomata. In review of the literature, the author finds only 8 other cases reported of the occurrence of such growths after endotracheal anesthesia. This is evidently a very rare complication of this form of anesthesia and is due to trauma caused by the tube. In the reported cases, as in the author's cases, the growths usually showed the characteristics of organizing hematomata, and were usually attached in the subglottic region.

COMMENT

We have seen instances of ulceration and swelling in the larynx and subglottic region caused by trauma from endotracheal tubes used in anesthesia. The difficulty became manifest within twenty-four hours and subsided within a few days whether tracheotomy was necessary or not. We would be a little sceptical of the etiology if the hoarseness did not develop for two months or more after the use of the endotracheal tube. L.C.McH.

Solitary Neurofibroma of the Larynx

G. E. Fisher and J. S. Odess (*Laryngoscope*, 59:1345, Dec. 1949) report 2 cases of solitary neurofibroma of the larynx and review the literature of the subject. They find that although neurofibromata arising from peripheral nerves occur frequently in various parts of the body, they are rarely seen in the larynx. The authors find only 19 cases reported in the literature, 9 by foreign authors, and 10 in the American literature. In most of the reported cases, the patients were in the third decade of life, although one patient was sixty years old, and one was a child four years of age. The symptoms varied, depending on the size and location of the growth, from mild hoarseness to severe dyspnea. In the authors' 2 cases, one patient was a man seventy-five years of age, who showed severe dyspnea when first seen, which he stated had been progressively increasing for several years; he also felt "a lump" in his throat. The tumor was located on the upper surface of the base of the left cord, and was removed under direct laryngoscopy. The second patient was a man twenty-three years of age; his chief symptoms were hoarseness and a dry cough; there was no dyspnea. The growth was located on the left aryepiglottic fold and was also removed under direct laryngoscopy. Both tumors were found to be benign neurofibromata. There has been no recurrence in either case; the first patient has been under observation for over five years since removal of the tumor.

COMMENT

An interesting report of a type of tumor which is rare in the larynx. ***L.C.McH.***

Iodine Solution With No Sting

Iodine has been established for many years as an efficient and versatile antiseptic. The solvent for the iodine has varied over the years but most commonly is found to be alcohol, water or a combination of the two. However, the use of alcohol causes irritation and pain when the antiseptic solution is applied to open wounds. On the other hand, an increase in the proportion of water increases the hazard of freezing of the solution under conditions of low temperature storage or shipping, a hazard manifested by the damage to surrounding materials should the bottles of solution freeze and crack.

In a paper read before the American Pharmaceutical Association Convention in Atlantic City, N. J., on May 3, 1950 Drs. Louis Gershenfeld and Bernard Witlin suggested a solution of iodine composed of 2 per cent iodine, 2.4 per cent sodium iodine, 25 per cent propylene glycol and distilled water. This solution has a high bactericidal efficiency, a free iodine content equivalent to the present-day iodine tincture, a low freezing point, and it does not sting nor irritate the skin. It also has a desirable adhesiveness to human skin and mucous membranes. The authors also stated that this solution is applicable not only to human and veterinary use but in food utensil sterilization, for the disinfection of thermometers, for water for human consumption, and in the disinfection of swimming pools.

Cepharanthine in Tuberculosis

Research in Japan toward a cure for tuberculosis has revealed that the alkaloid cepharanthine, found in the roots of *Stephania cepharantha* and the stems of *S. satakii*, has been effective in 48.8 per cent of 290 cases of human pulmonary tuberculosis. Some good results were obtained in tuberculosis of the bones and of the urogenital tract and excellent results in lesions of the eye. An editorial in *Brit. Med. J.* [No. 4648:294 (Feb. 4, 1950)] stated that the alkaloid was also effective as a prophylactic when 0.1 mg. was given daily for a week with a repeat of this course after a rest of one week. Among 2,869 persons so treated the rate of appearance of new cases of tuberculosis was 0.14 per cent during 8 months while among 37,040 untreated persons the new case rate was 3.48 per cent. The alkaloid may be given orally or intravenously. It has also shown effectiveness in the treatment of leprosy.

Medical BOOK NEWS

Edited by
ANDREW M. BABEY, M.D.

All books for review and communications concerning Book News should be addressed to the Editor of this department, 1313 Bedford Avenue, Brooklyn 16, N. Y. When books are sent to us with requests for review, selections for that purpose are promptly made.

JEAN MARTIN CHARCOT
1825 ~ 1893

Classical Quotations

● Let us commence with paralysis agitans . . . If you tell the patient to carry the glass to his mouth, you will see perhaps that the tremors augment a little in amplitude, but he will never produce those oscillations of large extent, which are characteristic of disseminated sclerosis.

JEAN MARTIN CHARCOT

Clinical Lectures on Diseases of the Nervous System. The New Sydenham Society. Translated by Thomas Savill. London, 1889.

Pediatrics

Mitchell-Nelson Textbook of Pediatrics. Edited by Waldo E. Nelson, M.D., with the collaboration of sixty-three contributors. 5th Edition. Philadelphia, W. B. Saunders Co., [c. 1950]. 4to. 1,658 pages, illustrated. Cloth, $12.50.

This most recent edition of the Mitchell-Nelson one volume System of Pediatrics is as complete, recent and authoritative as was the excellent fourth edition at its time of appearance.

The whole text has been rewritten and the following subjects are new or completely rewritten: Growth and Development, Congenital Malformations, Inborn Errors of Metabolism, Parenteral Fluid Therapy, Anesthesia for Children, Infection, Immunity and Allergy in Relation to Pediatrics, Streptococcal Infections, The Use of the Viral Diagnostic Laboratory, Individual Virus Diseases, Histo Plasmosis, Congenital Heart Disease, Mental Deficiency and Burns.

Each subject has been covered in a clear manner with a minimum of repetition by a nationally recognized authority in that particular subject. The list of authorities—sixty-three in number—is a roster of the names of some of the foremost workers, thinkers, and writers in the American Pediatric field.

Each subject is handled with such thoughful mastery that it may be easily understood by a nurse or medical student and yet thoroughly enjoyed by a fellow authority.

Mitchell-Nelson is probably the best and most up-to-date single volume System of Pediatrics available.

KENNETH G. JENNINGS

Nutrition

Rehabilitation Through Better Nutrition. University of Cincinnati Studies in Nutrition at the Hillman Hospital, Birmingham, Alabama. By Tom D. Spies, M.D., Philadelphia, W. B. Saunders Co., [c. 1947]. 8vo. 94 pages, illustrated. Cloth, $4.00.

This small volume emphasizes subclinical states of inadequate nutrition in deficiency diseases. It effectively points to the fact that deficiency states of long evolution do not necessarily reverse in dramatic fashion but require long-term application of well-known principles of nutrition. The ultimate goal of therapy is complete "rehabilitation" for work and living—a state of complete "dynamic balance" achieved by well-balanced nutrition. "In order to rehabilitate the person with nutritive failure we must remove, whenever possible, the causative factors and apply therapy that will not only correct the *specific* deficiency disease, but also restore completely the patient's nutritional status." The diet adequate for the normal individual will not suffice to restore the nutritional status of the malnourished person. Vitamins are only a part of the therapy in most deficiency states. Liberal calories, proteins and minerals are of equal importance.

GEORGE E. ANDERSON

—Continued on following page

MEDICAL BOOK NEWS

—Continued from preceding page

Cardiology

A Primer of Electrocardiography. By George E. Burch, M.D., and Travis Winsor, M.D. 2nd Edition. Philadelphia, Lea & Febiger, [c. 1949]. 8vo. 245 pages, illustrated. Cloth, $4.50.

This is the second edition of an excellent primer. It is reliable and very readable. Unipolar leads are considered superior and used in this edition.

ANDREW BABEY

Psychosomatics

Outwitting Your Years. By Clarence William Lieb, M.D. New York, Prentice-Hall, [c. 1949]. 12mo. 278 pages, illustrated. Cloth, $2.75.

This is a very sensible and readable book. The writer quotes Carrel as saying that "Leisure is even more dangerous for the old than for the young." He agrees but does not advise too much activity either. A good deal of the book is given to ways to occupy your time but the physical, health and disease, is not neglected. It is psychosomatic, if the emphasis is, properly, psycho. We recommend the book for those who need it.

WALTER D. LUDLUM, SR.

Obstetrics

A Treatise on Obstetric Labor. By Richard Torpin, M.D. Chapter on Erythroblastosis fetalis and the Rh factor by Edith L. Potter, M.D. and Philip Levine, M.D. Augusta, Ga., Augusta Obst. & Gyn. Book Co., [c. 1948]. 8vo. 590 pages, illustrated. Cloth, $7.00.

An up to date treatise on labor and its complications, the greater portion of which is devoted to complications, this work represents the author's experience and opinions along with a great amount of material from recent literature. It serves as an excellent reference book on current opinion. The author's opinions and treatment are on the conservative side. His ideas regarding delivery of patients in the doctor's office are interesting and unique. Illustrative cases are appended.

J. THORNTON WALLACE

Rehabilitation

Rehabilitation of the Handicapped. A Bibliography, 1940-1946. By Maya Riviere. In 2 volumes. New York, National Council on Rehabilitation, (Livingston, N. Y., Livingston Press), [c. 1949]. 8vo. 998 pages. Cloth, $10.00 for set of 2 volumes.

This work, affords a most complete listing of publications pertaining to rehabilitation of the handicapped for the period of 1940 to 1946 inclusive. Listing is first by alphabetical order of the authors or by title if a compilation. This listing fills all of volume one and part of volume two, and includes a brief word as to the nature of the article or text. It is followed by a listing of the authors and a listing of films representative of the subject, and their sources. A general index completes the cross indexing of the books. These volumes will prove to be of the greatest value to afford ready access to the pertinent literature for the period covered.

JEROME WEISS.

Questions

Medical State Board Questions and Answers. By R. Max Goepp, M.D. & Harrison F. Flippin, M.D. 8th Edition. Philadelphia, W. B. Saunders Co., [c. 1950]. Octavo of 663 pages. Cloth, $7.00.

This book should prove to be very useful for all men studying for State Board examinations, regardless of where these may be. It covers all the principal courses studied in medical school and does it simply and briefly by the use of questions and answers.

ANDREW BABEY

Clinical Pathology

Normal Values in Clinical Medicine. By F. William Sunderman, M.D. and Frederick Boerner, V.M.D. Philadelphia, W. B. Saunders Co., [c. 1949]. 4to. 845 pages, illustrated. Cloth, $14.00.

This volume comprises a great many normal values in the various specialties of medicine. There are 413 tables and considerable other text and some illustrations. Each specialist will find in an appropriate chapter the figures needed by him. Data such as these are invaluable and should be in the standard textbooks and monographs. Sunderman & Boerner, by gathering them in one volme, have provided the physician with an invaluable reference work. It should be in the library of every medical school and institution.

MILTON PLOTZ

Physics

Biological Reactions Caused by Electric Currents and by X-Rays. A Theoretical Study of the Phenomena of Excitation in the Nerve by Different Electric Currents and of the Biological Reactions Caused by X-Rays, Both Based Upon a Common Principle. By J. Th. Van Der Werff, M.D. New York, Elsevier Pub. Co., [1948]. 8vo. 203 pages, illustrated. Cloth, $4.00.

This little volume is a highly specialized treatise which concerns itself with the physics and mathematics of electrical and x-ray phenomena. Only advanced students, it would appear to the reviewer, could possibly understand this complicated work.

ANDREW BABEY

—Continued on page 346

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MEDICAL BOOK NEWS

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Obstetrics

Atlas of Obstetric Technic. By Paul Titus, M.D. Illustrated by E. M. Shackelford. 2nd Edition. St. Louis, C. V. Mosby Co., [c. 1949]. 4to. 197 pages, illustrated. Cloth, $7.50.

Replete with excellent drawings and diagrams, this *Atlas* should be well received by obstetricians. As a supplement to standard text books it is of great value. In addition to the excellent treatment of the subject in the first edition, this edition contains a section on pregnancy and prenatal care, also one on anaesthesia and analgesia. Considerable revision in the section on pelvimetry and forceps is to be noted. This book should prove of great assistance to the student as well as general practitioner and specialist.

WILLIAM C. MEAGHER

Physiotherapy

L'Ultra-Violet, La Lumiere Solaire et Artificielle. L'Infra-Rouge. (J. Aimard & H. Dausset). Edited by H. Aimes & P. Betoulières. 7th Edition. Paris, l'Expansion Scientifique Francaise, [1949]. 12mo. 231 pages, illustrated. Paper, 800 frs.

This book is a syllabus in four parts dealing with the use of sunlight, ultraviolet and infrared radiations. In Part One the mode of action of these therapeutic agents is discussed. The material is well presented. Part Two deals with the various types of apparatus used in therapy and will be of interest to the physiotherapist. Part Three describes the techniques to be followed when using sunlight, ultra-violet light and infra-red radiations. Part Four is devoted to therapeutic indications and results. The diseases for which these modalities may be used are arranged in alphabetical order for ready reference. The object of treatment, the technique and the results are discussed under each heading. It seemed to this reviewer that scientific accuracy was sometimes sacrificed to enthusiasm for the methods employed. This volume will be of interest to those concerned with physiotherapy in general hospitals, in rehabilitation centers and in health resorts.

EDWIN P. MAYNARD, JR.

Vitamins

Vitaminology. The Chemistry and Function of the Vitamins. By Walter H. Eddy, Ph.D. Baltimore, Williams & Wilkins Co., [c. 1949]. 8vo. 365 pages, illustrated. Cloth, $6.00.

Dr. Eddy has coined a new term to title this book. *Vitaminology* only indicates that vitamin research, a field which not many years ago was limited to the recognition of the existence of a few accessory food factors, has developed into a discipline concerned with the elucidation of mechanisms in hormonal and enzymatic systems.

Casimir Funk has written a fascinating foreword in which he presents some intriguing problems for future investigations such as "gamma" vitamins and the possible role of still unidentified vitamins in neoplastic growth and vascular degeneration.

Dr. Eddy has brought into this volume the essential up-to-date data, describing the functions of each identified vitamin, the syndromes associated with their deficiency states, methods for assay, the chemistry of these agents and their role in therapy.

It is an important book, well written and makes fine reading.

WILLIAM S. COLLENS

Biochemistry

Clinical Biochemistry. By Abraham Cantarow, M.D. & Max Trumper, Ph.D. 4th Edition. Philadelphia, W. B. Saunders Co., [c. 1949]. 8vo. 642 pages, illustrated. Cloth, $8.00.

This book is the 4th edition of a well established text on *Clinical Biochemistry.*

The authors have added new material relating to kidney and liver function with detailed lipid and jaundice metabolism. The biochemical findings in shock and adrenal functions are discussed.

The mineral metabolism is brought up-to-date including potassium therapy in diabetes.

Acid-base balance, respiratory regulation and anoxia have a prominent place in this edition. An appropriate bibliography is appended to each chapter.

The reviewer recommends this book.

MORRIS ANT

Physiology

Temperature and Human Life. By C. E. A. Winslow & L. P. Herrington. Princeton, Princeton University Pr., [c. 1949]. 8vo. 272 pages, illustrated. Cloth, $3.50.

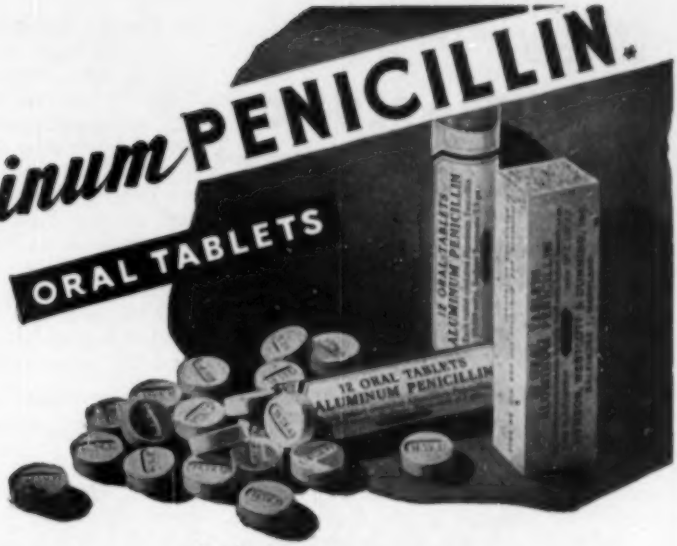
No one probably should be more interested in the internal and external temperature of the human body and the effects of environmental temperatures upon the heat production and heat loss of the body than physicians. This volume is a thorough review and discussion of the whole subject, with a special attempt to suggest methods of modifying the effects of climate upon the life of man so that his activity may reach its greatest functional capacity regardless of the region he inhabits.

The most effective aids in conditioning of homes and the types of clothing most efficient in conserving heat or in cooling are covered. The most recent types of calorimetry are described. The book is well worth study by all forward looking physicians.

KENNETH G. JENNINGS

Aluminum PENICILLIN.

ORAL TABLETS



Greater effectiveness

Oral therapy with Aluminum Penicillin has proved to be effective in fulminating infections such as pneumonia[1] and in other infections due to streptococci, staphylococci and gonococci.[2] It rarely causes gastric disturbance or allergic reactions. The patient's bodily and mental comfort is improved because the necessity for frequent injections is eliminated.

The unique advantages of Aluminum Penicillin are that it is not soluble in solutions of acidity corresponding to that of gastric secretion, but is gradually converted into a readily absorbed form in the intestinal tract. These factors provide for maximum utilization of the dosage administered, higher and more prolonged blood levels.[3]

Sodium benzoate is added because it inhibits the destructive action of intestinal enzymes.[4]

Oral Tablets

Each tablet contains: Aluminum Penicillin, 50,000 units; sodium benzoate, 0.3 gram. Supplied in vials of 12 tablets.

[1]Terry, L. L. and Friedman, M. The Military Surgeon, Vol. 103, No. 5, November, 1948.
[2]Friedman, M. and Terry, L. L. Southern Medical Journal, Vol. 42, No. 6, June, 1949.
[3]Bohls, S. W. and Cook, E. B. M. Texas State Journal of Medicine, Vol. 41, November, 1945, p. 342.
[4]Reid, R. D., Felton, L. C. and Pitroff, M. A. Pro. Soc. for Exp. Biol. and Med., Vol. 63, 1946, p. 438.

* Patent applied for.

HYNSON, WESTCOTT & DUNNING, INC.
Baltimore, Maryland

Modern THERAPEUTICS

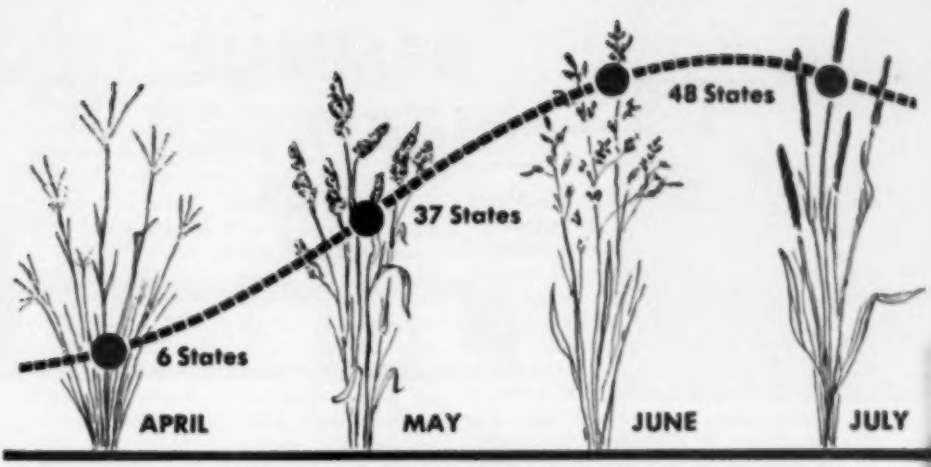
Development of Resistant Falciparum Malaria Strains to Proguanil

Proguanil has shown great value in the treatment and suppression of falciparum malaria. Early trials showed that 100 mg. a day would protect persons bitten repeatedly by infected mosquitos and that heavy infections could be cured by a 10-day course of 300 mg. a day. However, as the use of this drug became more worldwide it became evident that there was variation in the response of different strains of the parasites to the drug. Edeson and Field reported in the *Brit. Med. J.* (No. 4646:147 (Jan. 21, 1950)) that in the Tampin district of Malaya resistance to the drug began to appear after about 2 years of use. Proguanil had been used widely in that area but probably sporadically for the suppression of malaria. In 1947 a single dose of 100 to 300 mg. of proguanil had been completely effective as a curative dose in infections. Two years later one out of every 4 failed to respond to a standard course of 300 mg. a day for 5 days. The authors suggest that unless this problem of resistance development can be overcome the important role which this drug has won in the treatment of malaria may be lost.

Chlorcyclizine in the Treatment of Allergies

Chlorcyclizine (Perazil), having the chemical formula N-methyl-N'-(4-chloro-

—Continued on page 54a



This graph shows the number of States where hay fever, due to grass, prevails during the Spring and early Summer months.

Dreaded Season...

Many hay fever sufferers now are entering what is ordinarily their most uncomfortable season. Fortunately, more and more patients each year are enjoying the therapeutic benefits of Neo-Antergan® Maleate. Because of its safe and, in many cases, strikingly effective action in relieving the distressing symptoms of allergy—Neo-Antergan has become a favorite antihistaminic with physicians and patients.

Neo-Antergan is advertised exclusively to the medical profession. Your patients can secure its benefits *only through your prescription.*

Complete information concerning Neo-Antergan Maleate and its clinical uses will be sent on request.

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MALEATE

(Brand of Pyranisamine Maleate)

(N-*p*-methoxybenzyl-N′, N′-dimethyl-N-α-pyridylethylenediamine maleate)

COUNCIL ACCEPTED

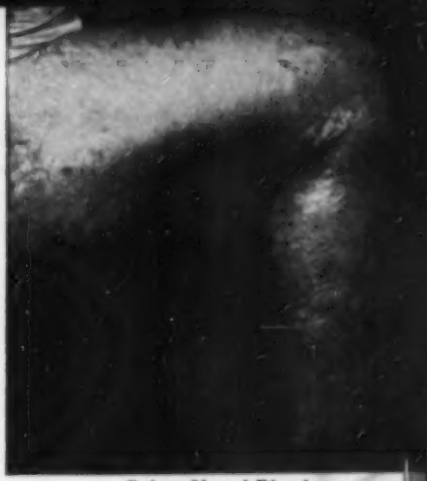
MODERN THERAPEUTICS

—Continued from page 52a

benzhydryl) piperazine dihydrochloride was used in the treatment of various allergies, including hay fever, urticaria, dermatitis, vasomotor rhinitis, bronchial asthma, and sinusitis. There was an overall clinical improvement in 94 per cent of the common allergic symptoms. Jaros stated in *Ann. Allergy* (7:466 (1949)) that a daily dose of 50 mg. was given to all adult patients in one oral dose. A dose of 25 mg. in children 8 to 12 years of age gave results comparable to 50 mg. in adults. The least satisfactory results were obtained in the patients with bronchial asthma. In hay fever, urticaria, atopic and contact dermatitis and sinusitis there was excellent improvement in 100 per cent of the cases. Toxic side effects were observed in only 4.8 per cent of the cases, the chief symptom being drowsiness. Many of the patients had had previous experience with other antihistaminics, but expressed preference for Perazil. The author was enthusiastic about the compound expressing the belief that it was less toxic, of longer duration of action and more effective than other antihistaminic compounds.

—Continued on page 58a

SUMMER PSORIASIS CALLS FOR RIASOL



Before Use of Riasol

After Use of Riasol

The actinic rays of summer sunlight may aggravate many cases of psoriasis. In addition, the humiliation resulting from exposure of the ugly patches makes effective treatment imperative.

The unique chemical combination of mercury with soaps in RIASOL penetrates the stratum corneum and brings the therapeutic agent in direct contact with the psoriatic lesions in the deeper layers of the skin.

Usually with the use of RIASOL, the unsightly red patches and the obnoxious silvery scales soon start to disappear. In many cases the skin patches clear completely and there are prolonged remissions.

RIASOL contains 0.45% mercury chemically combined with soaps, 0.5% phenol and 0.75% cresol in a washable, non-staining, odorless vehicle.

Apply daily after a mild soap bath and thorough drying. A thin, invisible, economical film suffices. No bandages necessary. After one week, adjust to patient's progress.

RIASOL is ethically promoted. Supplied in 4 and 8 fld. oz. bottles at pharmacies or direct.

Mail coupon today for your free clinical package. Prove RIASOL in your own practice.

MAIL COUPON TODAY—TEST RIASOL YOURSELF

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Please send me professional literature and generous clinical package of RIASOL.

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City ..... Zone ..... State .....

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RIASOL for PSORIASIS

practical ideals in diabetes

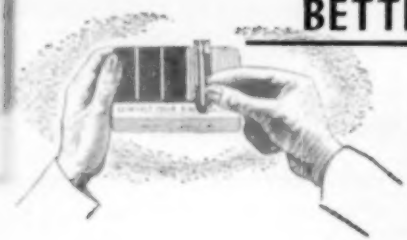
EARLY DIAGNOSIS

"The ideal detection center is in the private physician's office."[1] This approach to widespread early diagnosis of diabetes can be practical when *every routine examination of every patient includes urine-sugar analysis.* Routine analysis, in turn, is more practical for the physician who uses *Clinitest* (Brand) Reagent Tablets. The test is simple, rapid and self-contained (no external heating). Results are known at once

CLINITEST

REAGENT TABLETS ***for urine-sugar analysis***

BETTER CONTROL



"Generally, only the well controlled diabetic patient may expect to live to normal expectancy and without premature arterial degeneration."[2] Here too, practicality recommends *Clinitest.* The *Clinitest* (Brand) Urine-sugar Analysis Set (a compact pocket unit) enables the patient, under the physician's guidance, to make regular checkups simply, accurately and conveniently. This is a practical guarantee of the patient's cooperation without which adequate control by the doctor is hardly feasible.

Clinitest, reg. trademark

Bibliography: (1) Wilkerson, H. L. C.: New York State J. Med. *49*:2945 (Dec. 15) 1949. (2) Sweeney, J. S.: Texas State J. Med. *45*:623 (Sept.) 1949.

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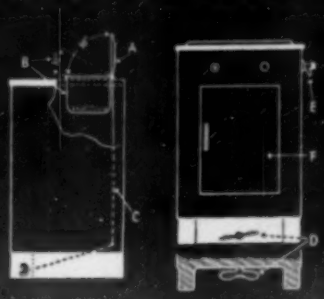
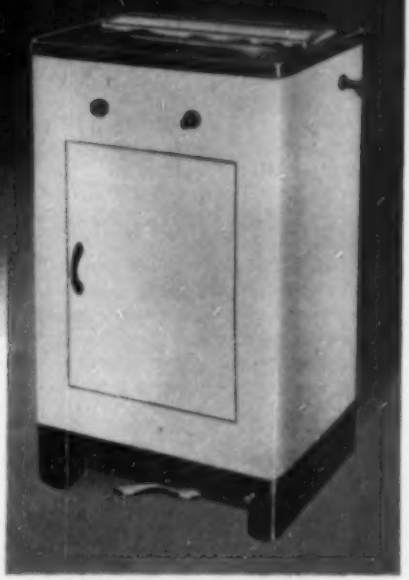
AMES COMPANY OF CANADA, LTD., TORONTO

Ultra-Modern in every detail





"American" CABINET MODEL
SMALL INSTRUMENT STERILIZERS

combine *exclusive* highlights in design and construction that insure greater operating safety, convenience and long periods of satisfactory service.

(a) **Cover** – fabricated of stainless steel and elevating to full 90° angle to permit easy removal of tray without interference.

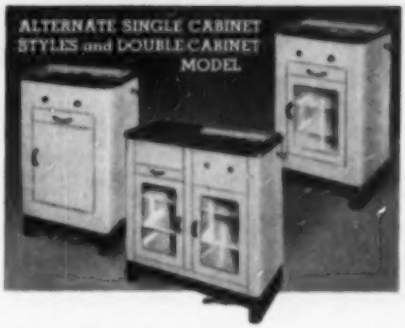
(b) **Cover** – elevates to 30° angle before immersed tray starts to raise, thus enabling operator to observe water level at all times to insure immersion of instruments.

(c) **Cover Elevating Mechanism** – Concealed entirely within cabinet, thus allowing cabinet to be placed flush against the wall.

(d) **Recessed Foot Pedal** – Eliminates tripping annoyances and permits greater freedom of access for operator.

(e) **Drain Faucet** – a special screw-type valve which will not stick or score and may be taken apart instantly for cleaning without tools.

(f) **Doors** – Solid double-panel or glass, hung on fully concealed steel hinges, fitted with Bakelite handle, spring catches and rubber bumpers.



BURN-OUT-PROOF!
An automatic safety measure protecting both Sterilizer and instruments against possible damage due to depletion of water supply in chamber.

ASK YOUR DEALER or write us for further information

AMERICAN STERILIZER COMPANY
Erie, Pennsylvania

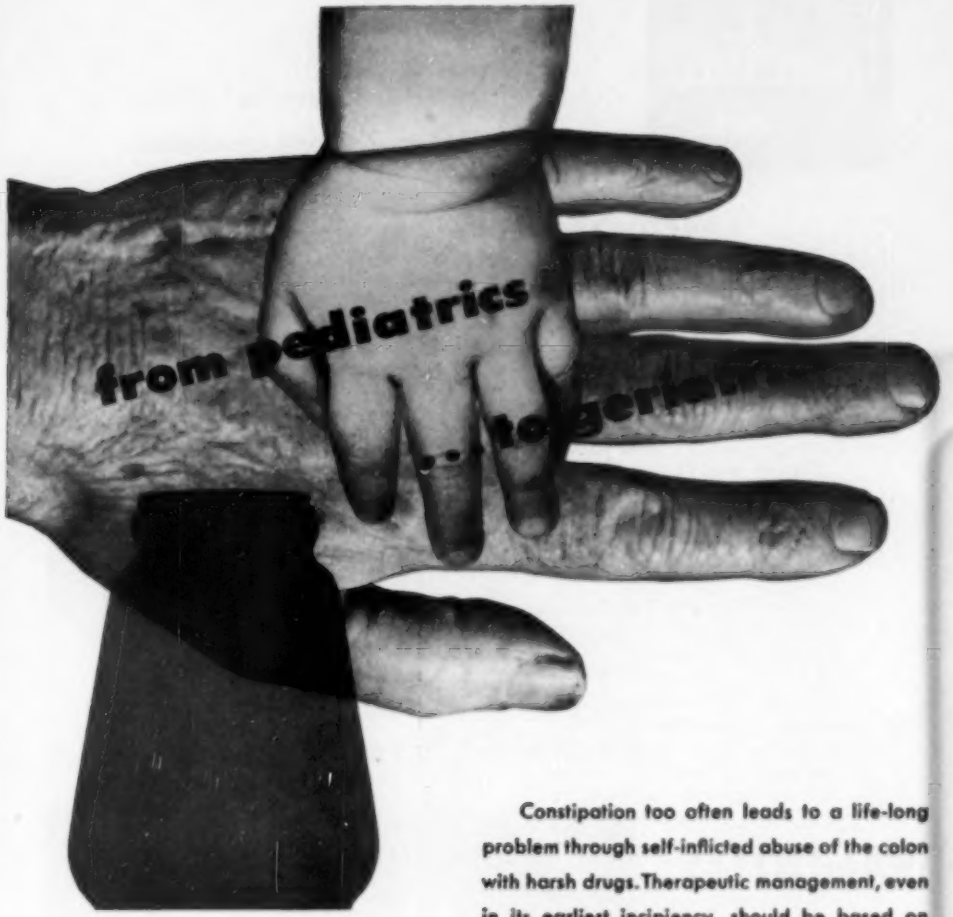
MODERN THERAPEUTICS

—Continued from page 54a

Tonicity of Penicillin and Streptomycin Solutions

Studies were conducted to determine the freezing point depression of solutions of sodium penicillin and of streptomycin in order to adjust solutions of these antibiotics to isotonicity for either collyria or parenteral therapy. Michaels reported in *Pharm. J.* (164:95 (Feb. 4, 1950)) that the potency of the commercial batches of sodium penicillin varied from about 1100 to 1400 units per mg. Therefore, the tonicity of sodium penicillin solutions would vary with the units per cc. concentration of the solution and also with the potency of the salt from which it was made. The author thus experimentally developed a nomogram showing the relationship between these two concentration factors and freezing point depression. A few factors taken from this graph are as follows: 50,000 units per cc. made from 1400 units per mg. salt has a FPD of 0.45°C.; 50,000 units per cc. made from 1200 units per mg. salt has a FPD of 0.56°C.; 20,000 units per cc. made from 1400 units per mg. salt has a FPD of 0.18°C.; 20,000 units per cc. made from 1200 units per mg. salt has FPD of 0.22° C.; 10,000 units per cc. made from 1400 units per mg. salt has FPD of 0.09° C.; and 100,000 units per cc. is hypertonic for any of the salt concentrations.

A graph was not prepared for other penicillins or for streptomycin but statements were made by the author that 77,000 units per cc. of crystalline sodium penicillin G and 98,000 units per cc. of benzyl penicillin each has a FPD of 0.56°C. A 2 per cent solution of streptomycin hydrochloride has a FPD of 0.56°C. and a 1 per cent solution has a FPD of 0.30° C. An 8 per cent solution of streptomycin sulfate has a FPD of 0.56°C. while a 1 per cent solution has a FPD of 0.08°C.



Constipation too often leads to a life-long problem through self-inflicted abuse of the colon with harsh drugs. Therapeutic management, even in its earliest incipiency, should be based on measures which neither disrupt normal bowel physiology nor favor cathartic addiction.

Zymenol is effective in preventing, as well as breaking, the cathartic habit. Zymenol promotes normal bowel function without purgation, without irritation and without the risk of fecal impaction. Zymenol is safe. Zymenol is mild. Zymenol is non-habit forming (the dose can be consistently reduced). Moreover, Zymenol is effective.

Zymenol is a colloidal emulsion of a special aqueous culture of Brewers Yeast (no live cells), with mineral oil as the lipid phase. Write for FREE 14 oz. ($1.25) trade package for your professional use.

Zymenol®

AN EMULSION WITH BREWERS YEAST

OTIS E. GLIDDEN & CO., INC., EVANSTON, ILLINOIS

FOR EFFECTIVE BOWEL MANAGEMENT

immediate relief within hours itching, burning halted; within 3 to 6 days discharge ceases.

speedy recovery 2 to 7 WEEKS average in vaginitis; within 5 weeks in cervicitis (postoperative)

westhiazole vaginal embodies every proven modern requirement for rapid control of infective vaginitis and cervicitis ..great buffering capacity • rapid restoration of normal vaginal pH • carbohydrates for growth of friendly Doderlein bacilli • control of secondary as well as primary infections to accelerate healing. There is nothing more . . .

effective, simple, dainty, convenient in **vaginitis and cervicitis**

VAGINITIS

CERVICITIS

westhiazole vaginal

single • dose applicators

WESTHIAZOLE VAGINAL: a sterile jelly containing 10% SULFATHIAZOLE, 4% UREA, 3% LACTIC ACID, 1% ACETIC ACID in a polyethylene glycol base. Non-irritant, non-toxic.

Samples and literature on request

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How Pet Milk Helps in Your Fight Against Disease

What is more important to the newborn infant than clean, safe food? Is not this your first concern when choosing a milk for your infant patients?

When you use Pet Evaporated Milk for infant formula, you are assured of a completely safe formula, as if there were no germs of disease in the world. Pet Milk is heat-sterilized in its sealed container, protected permanently from any source of contamination prior to actual consumption.

You are assured, too, that safe Pet Milk retains all of the food values that the best of milk can be depended upon to supply, and that these food values are uniform wherever and whenever Pet Milk is purchased.

Try Pet Milk for the babies in your care! Let this safe low-cost milk help you in your continuous fight against disease.

Favored for Infant Formula

PET MILK COMPANY, 1483-G Arcade Bldg., St. Louis 1, Mo.

News and Notes

Medical Research in the Last Half of the Twentieth Century

The above title was the theme of the symposium held as part of the ceremonies dedicating the new laboratory building of the Sterling-Winthrop Research Institute at Rensselaer (N.Y.) on May 17, 1950. Dr. Maurice L. Tainter, director of the Institute, presided at the symposium. James Hill, Jr. dedicated the building to the "advancement of human welfare" and Dr. Theodore Klumpp, president of Winthrop-Stearns, and Gov. Thomas E. Dewey, of New York, addressed the evening dinner meeting.

The speakers at the symposium were Prof. Otto Loewi, New York University College of Medicine; Dr. Wendell M. Stanley, University of California; Prof. Albert Szent-Gyorgyi, Institute for Advanced Study, Princeton, N. J.; Dr. Rene J. Dubos, Rockefeller Institute for Medical Research; Dr. Cornelius Rhoads, director, Sloan-Kettering Institute for Cancer Research; and Dr. William Dock, Long Island College of Medicine. The first three speakers named were Nobel Prize recipients.

Dr. Szent-Gyorgyi spoke of the need for continued pure research into the role of muscles in life, growth and degeneration. He stated that study in this direction had already shown that muscles are involved in a number of major diseases. The failure of muscles is the immediate cause of death in every second man in America. Dr. Szent-Gyorgyi noted that hypertension is related to muscle since the muscles of the small blood vessels contract and cause the blood pressure to rise. Also, since all tissue functions according to the same general pattern it is hoped that pure research into

—Continued on page 66a

"One-third to two-thirds *of all patients who seek medical help have as the most significant cause of ill health an emotional or neurotic disturbance . . . nervousness and fatigue are among the commonest symptoms.*"[1]

1. Wilbur, D. L.: J.A.M.A. 141:1199 (Dec. 24) 1949

NEW! SEDATIVE NUTRITIONAL SUPPORT SUPPLYING VITAMIN B_{12}

BĒPLETE®

ELIXIR VITAMINS B-COMPLEX WITH PHENOBARBITAL

Wyeth

Each teaspoonful (4 cc.) contains:

Phenobarbital	0.25 grain
WARNING: May be habit forming.	
Vitamin B_1	1.5 mg.
Vitamin B_2	1.0 mg.
Vitamin B_6	0.33 mg.
Vitamin B_{12}	1.66 mcg.
Niacinamide	10.0 mg.
Pantothenyl Alcohol	0.2 mg.

Alcohol 15%

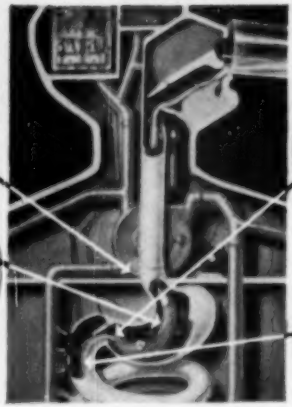
IN A DELIGHTFULLY APPETIZING WINE BASE

Wyeth Incorporated • Philadelphia 3, Pa. Wyeth®

Give faster pain relief with BUFFERIN

ACTS TWICE AS FAST AS ASPIRIN

WITHOUT GASTRIC DISTRESS!



1. BUFFERIN enters the stomach here.

2. BUFFERIN exerts its antacid effect, lessening the possibility of gastric distress.

3. BUFFERIN helps dilate the pyloric valve, promptly leaves the stomach.

4. BUFFERIN'S analgesic component is absorbed into the blood *twice as fast as aspirin*, relieves pain.

When you prescribe BUFFERIN to your patients you assure *faster relief of pain*. Clinical studies[1] show that within ten minutes after BUFFERIN is ingested, blood salicylate levels are as great as those attained by aspirin in twice this time. That is why BUFFERIN *acts twice as fast as aspirin*.

BUFFERIN has *greater gastric tolerance*. BUFFERIN'S antacid ingredients provide protection against the gastric distress so often seen with aspirin.[1] BUFFERIN, therefore, is especially suited for use when prolonged use of salicylates is indicated.

1. Effect of Buffering Agents on Absorption of Acetylsalicylic Acid J. Am. Pharm. A., Sc. Ed. 39:21, Jan. 1950.

In vials of 12 and 36 and bottles of 100. Scored for divided dosage. Each BUFFERIN tablet contains 5 grains of acetylsalicylic acid with optimal proportions of magnesium carbonate and aluminum glycinate.

BUFFERIN
is a trade-mark of the Bristol-Myers Company

A product of BRISTOL-MYERS COMPANY
19 West 50 St., New York 20, N. Y.

—Continued from page 62a

the role of muscle will provide some of the answers to questions about cancer, polio, rheumatic fever, and arthritis.

Dr. Loewi ventured to state a hope that within a relatively short span of time, science shall be able to produce a cure for all disease produced by micro-organisms. The reason for this hope is based, at least partially, upon the relatively large number of therapeutic agents which have been discovered despite the short period of time since the first assault was launched against the viruses. Although the knowledge is still meager, discoveries of the mechanism of drug action on cells has opened significant avenues of approach for the exploration of basic mechanisms. Dr. Loewi pointed out that he felt that one of the most significant advances in medicine was the discovery of drugs poisonous to microbes but not poisonous to the cells of the host. Another discovery that has proven to be very fruitful is the concept of metabolic antagonism. The activity of enzymes may be blocked by the competition of chemical agents which structurally resemble prosthetic groups of the enzymes. Such a mode of action is exhibited by the sulfonamides and thus explains their deleterious effects on micro-organisms. One of the basic problems confronting microbiologists, Dr. Loewi stated, is that of cell permeability. Cell nutrients, such as glucose, must reach the interior of the cell. How this is accomplished is unknown, but it is known that it is an active energy yielding process, which controls the cell permeability. How the energy needed to

—Continued on page 68a

NEWS AND NOTES

—Continued from page 66a

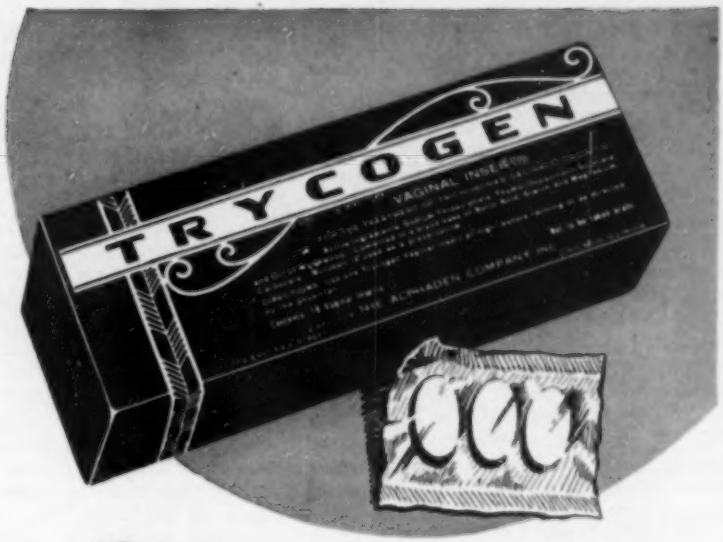
change the permeability of the cell is liberated by contact between the nutrient and the cell is not known, but when more is learned of this mechanism it may throw light upon the mechanism by which drugs act.

In principle, Dr. Loewi stated that pure research has an objective to establish general laws which may be applied on a broader basis, leading to the recognition of new phenomena, and pharmacological research aims at exploring organismic structures and functions through the study of their changes as produced by chemical agents.

Dr. Stanley said that the main objective of virus study is to find the exact nature of the difference between virulent virus strains which produce disease in human beings and avirulent strains. Studies on the tobacco mosaic virus has revealed that these viruses are characterized by their components of virulent germs for injection into human beings to produce resistance to infection. Once the immunizing substances small size, by their ability to reproduce or multiply within the living cells of a host, by their ability to change or mutate during multiplication, and by their inability to reproduce or grow on artificial media or in the absence of specific living cells. More than 300 different viruses capable of producing disease in man, animals and plants have been discovered, he said. The few viruses which have been obtained in highly purified form were found to have a composition and properties that are characteristic of organisms rather than of molecules. The solution of the mystery as to the manner in which viruses reproduce may represent the fundamental process by which all living cells reproduce.

Dr. Dubos stated that he felt that science is on the threshold of achieving the means for immunity to infectious diseases such as tuberculosis, meningitis, influenza, and pneumonia. New developments have resulted in the synthesization of selected

—Continued on page 70a



The "DRY TREATMENT" OF VAGINITIS

Comforting to the patient, simple and clean to administer, is the "dry treatment" of vaginal leukorrhea, using—

1. **TRYCOGEN POWDER** insufflation in the office; (optional)
2. **TRYCOGEN INSERTS** for home treatment

In trichomonal, monilia, or senile vaginitis, TRYCOGEN acts to destroy the parasitic invaders, relieve the pruritus, and restore the normal vaginal flora.

TRYCOGEN presents sodium thiosulfate, thymol, oxyquinoline sulfate and oil of wormwood in a base of boric acid and starch. Non-irritating; non-staining.

Trycogen Inserts, Boxes of 18 and 100 • Trycogen Powder, 25-gram vials. Also in 8-oz. and 16-oz. containers.

THE ALPHADEN COMPANY

CHICAGO, ILLINOIS

—Continued from page 68a

specific for each infectious agent have been isolated it becomes theoretically possible to determine the chemical structure and the nature of the groups which direct the immune reactions. Subsequently, the chemical synthesis of the active determinant groups and immunization with synthetic antigens becomes possible. To substantiate these statements Dr. Dubos pointed out that the injection into experimental animals of certain conjugates of aldobionic acids, which are components of the capsular substances of virulent pneumococci, has been found to elicit in these animals a definite level of immunity against infection with pneumococci.

Dr. Dubos declared that it is unlikely to assume that it will be possible to achieve eradication of infectious by sanitation and antimicrobial therapy only. Instead, he foresaw that there would be a shift of emphasis in medical research to prevention with particular study of the physiological and biochemical disturbances which result in the state of the disease and of the multiple inter-reactions by which the host and parasite influence each other.

Dr. Dock spoke of the need for clinicians to learn to work in teams rather than in isolation or informal association. He suggested that small teams of family doctors and of specialists should be organized in each community in order to give the American people the best medical care and to give much consideration to preventing disease as well as curing it. Unless the medical profession develops a program of medical attention for the entire nation the problem will be taken out of the hands of physicians. He suggested that financing of such a program, without government operation, might be accomplished by compulsory insurance similar to that for automobile liability.

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Advertisements under the headings listed are published without charge for those physicians whose names appear on the MEDICAL TIMES mailing list of selected general practitioners. To all others the rate is $3.50 per insertion for 30 words or less: additional words 10c each.

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Assistants	Books
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ASSOCIATE in general practice wanted. Am located in middle of Bright Leaf Tobacco section. Money good and work isn't hard. Box 7A46, Medical Times.

ASSOCIATE for general practitioner. Percentage. Ohio license required. Well equipped office. Box 7A45, Medical Times.

DESIRE: PSYCHIATRIST, with board qualifications for location in building with other doctors. Opportunity and hospital facilities excellent. Calif. Personal interview required. Box 7A44, Medical Times.

GENERAL PRACTITIONER desires assistant; reasonable starting pay and worthwhile future. Located in nice suburb of Pittsburgh, Pa. Box 7A50, Medical Times.

GOOD TERRITORY for young physician interested in rural practice in Chesapeake Bay area. Opportunity to step into an established practice. Box 7A49, Medical Times.

OFFICE NURSE; experienced; knowledge of typing; excellent salary. Northern N. J. General practitioner. Box 7A47, Medical Times.

OPHTHALMOLOGIST wanted; to locate in fast growing medical center in prosperous, small, midwestern city. Partnership open to right individual. Box 7A41, Medical Times.

OPPORTUNITY, without salary with F.A.C.P. for study and practice of Gerontology. Object: affiliation. Chicago. Box 7A43, Medical Times.

—Continued on following page

POSITION as resident physician. Yellowstone National Park. Apartment furnished, as well as all equipment and supplies. Available July 1st, Oct. 1st. Box 7A42, Medical Times.

WANTED (Equipment, Homes, etc.)

INTERESTED in buying medical gadgets. Instruments of practical value for physical diagnosis or for treatment. Also interested in any ideas along this line. Making a collection. Box 7B7, Medical Times.

WISH TO PURCHASE recent model Cameron Cauterodyne. Medium size (office size). Must be in good condition and a bargain. Box 7B8, Medical Times.

WANTED (Locations, Positions, etc.)

CERTIFIED in medicine & allergy; married—2 children. Age 42; good health. Experience as medical director of insurance company. Could assist in part-time work with small insurance co. Texas. Box 7C10, Medical Times.

PHYSICIAN, 35, married, wishes association with busy surgeon or preceptorship. Has 9 years general practice, 2 year internship. Prefer man within 20 mile radius of Newark, N. J. Box 7C8, Medical Times.

DESIRE TO PURCHASE active eye practice near N. Y. C. Will consider partnership. Can make substantial investment. Box 75C7, Medical Times.

GENERAL PRACTITIONER (interested in pediatrics) for past 9 years, would like to join a medical group in Nassau or Suffolk County. Box 7C9, Medical Times.

PRECEPTORSHIP or assistantship wanted with either a plastic surgeon or general surgeon or other surgical specialty by 35 year old married G.P. 8 years G.P. Practice successful—but wants to specialize. Box 7C11, Medical Times.

WANTED (Miscellaneous)

WISH TO PURCHASE: Ewing, J., "Neoplastic Diseases," 1940, Saunders; Joseph Needham, "Chemical Embryology," 3 vols., Cambridge. Box 7D7, Medical Times.

FOR SALE (Practices)

COMBINED office-residence with general practice for sale in growing L. I. suburban community. Leaving to specialize. Box 7F17, Medical Times.

LUCRATIVE general practice for sale. Home and office combination in southern N. J. Wish to leave to specialize. Can stay as long as necessary to introduce. Box 7F16, Medical Times.

PRACTICE and 1½ yr. old, 23 room medical bldg. for sale. 10 rooms fully equipped. $50,000 industrial, general and surgical practice. Ideal setup for 3-4 man group practice. No.-East Ohio. City of 30,000. Box 7F15, Medical Times.

WELL ESTABLISHED practice and fully equipped office being offered to qualified M.D. Ill health is reason for leaving present location. Los Angeles, Calif. Phone MA 6-7017 or write Box 7F14, Medical Times.

60% INTEREST in small clinic for sale. Arizona. Box 7F13, Medical Times.

FOR SALE (Homes, Sanataria, etc.)

MIAMI BEACH, Fla. Completely equipped medical office, long established in exclusive section. Ready for immediate practice. Price less than first year's income. Terms. Personal reasons for selling. Would consider Locum Tenens. Box 7E8, Medical Times.

FOR SALE: Medical office bldg. in southern Cal. Non-metropolitan area, in town of about 5,000. Not close to city. Box 7E7, Medical Times.

FOR SALE OR RENT—28 bed, licensed convalescent home on 3 acre tract of land in southern Conn. Excellent retirement income on small down-payment with monthly installments from income. Details by writing: Box 179, Wallingford, Conn., or Box 7E9, Medical Times.

FOR SALE (Equipment)

CAMBRIDGE portable, string portable electrocardiograph. Excellent condition. $350. N. J. Box 7G37, Medical Times.

COLONIC IRRIGATION table, fully equipped with inlet & drain for plumbing installation. Box 7G35, Medical Times.

FOR SALE: Ruddick peritoneoscope, complete with walnut case—used only a few times—excellent condition—any reasonable offer accepted. Box 7G34, Medical Times.

HIGH COLONIC APPARATUS for sale. Very reasonable. Box 75G23, Medical Times.

NATIONAL PROCTOLOGY SET complete with case and new rheostat, $50.00. Original cost 6 months ago, $84.00. Box 7G33, Medical Times.

McCASKEY medical filing cabinet for sale; pre-war; good condition. Make an offer. Illinois. Box 7G38. Medical Times.

FOR SALE (Miscellaneous)

16MM. CINE KODAK magazine-type movie camera. New, never used. $150. Cash. Box 7H3, Medical Times.

FOR RENT (Offices, etc.)

CAL. MED. BLDG., 1401 S. Hope St., L. A., Cal. Sublease 4 rm. suite, lab. and sell G.P. office equipment. Reception room, consultation room, 2 treatment rooms, short wave and infra-red lamps, 2 steel suspension files with locks, 2 typewriters, etc. Sacrifice. No charge for practice. Rent reasonable. Box 7R16, Medical Times.

VACANCY, suite of 4 rooms. Desirable location for dentist. Joseph Halton Hospital Bldg., Sarasota, Fla. Write Joseph Halton, M.D., at above address, or Box 876R14, Medical Times.

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RUDOLPH R. GARSON, M.D. Offices now located at 2461 Ocean Avenue, Brooklyn 29, N. Y. Office hours: 1-2; 6-7:30.

MEDICAL (advertisers index) TIMES

JULY, 1950

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Cehistra is available in bottles of 10 effervescent tablets, each containing 10 mg. of prophenpyridamine (available as the maleate), 100 mg. of vitamin C, and 320 mg. of aspirin in an alkalizing base consisting of sodium bicarbonate (1820 mg.), calcium hydroxide, and citric acid.

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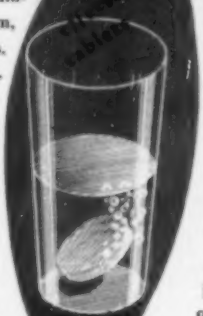

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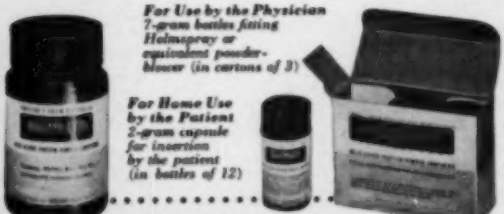

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